excess of the lubricants. Generally, drugs having strong bitter taste are coated with a suitable coating agent for masking the bitter taste. However, this method has a problem in that further research is needed to secure physical strength of plain tablets for smooth progress of related processes and costs can increase due to increase in number of processes.

• Therefore, there is a need for a pharmaceutical composition for oral administration, which can prevent failure in tableting besifovir dipivoxil or a pharmaceutically acceptable salt thereof while providing masking of bitter taste of the besifovir dipivoxil or the pharmaceutically acceptable salt thereof.

【Disclosure】

【Technical Problem】

• Examples of the present disclosure provide a method, granules or composition which can prevent difficulty in production due to stickiness of besifovir dipivoxil or a pharmaceutically acceptable salt thereof upon compression molding while masking bitter taste and thus improving compliance to administration.

【Technical Solution】

• One example of the present disclosure relates to bitter taste-masked granules comprising besifovir dipivoxil or a pharmaceutically acceptable salt thereof, coated with a lipid excipient.

• In one aspect, the present disclosure refers to bitter taste-masked granules comprising besifovir dipivoxil or a pharmaceutically acceptable salt thereof, and being coated with a lipid excipient, wherein the lipid excipient is at least one fatty acid ester selected from the group consisting of glycerol distearate, glyceryl stearate, glyceryl oleate, glyceryl myristate, cetyl palmitate, cetyl caprate, stearyl palmitate, and stearyl stearate.

• Another example of the present disclosure relates to a method of preparing bitter taste-masked granules comprising besifovir dipivoxil or a pharmaceutically acceptable salt thereof, the method comprising: melting a lipid excipient through heating to a temperature higher than or equal to a melting point of the lipid excipient; mixing the melt with solid state besifovir dipivoxil or the pharmaceutically acceptable salt thereof ; and cooling the mixture.

• In another aspect, the present disclosure refers to a method of preparing bitter taste-masked granules comprising besifovir dipivoxil or a pharmaceutically acceptable salt thereof, and being coated with a lipid excipient, the method comprising: melting the lipid excipient through heating to a temperature higher than or equal to a melting point of the lipid excipient, wherein the lipid excipient is at least one fatty acid ester selected from the group consisting of glycerol distearate, glyceryl stearate, glyceryl oleate, glyceryl myristate, cetyl palmitate, cetyl caprate, stearyl palmitate, and stearyl stearate; mixing the melt with the besifovir dipivoxil or the pharmaceutically acceptable salt thereof in a solid state; and cooling the mixture.

• A further example of the present disclosure relates to a pharmaceutical composition comprising: bitter taste-masked granules comprising besifovir dipivoxil or a pharmaceutically acceptable salt thereof, coated with a lipid excipient; and a pharmaceutically acceptable additive.

• In another aspect, the present disclosure refers to a pharmaceutical composition comprising: the bitter taste-masked granules as disclosed herein; and a pharmaceutically acceptable additive.

Yet another example of the present disclosure relates to a method of preparing a pharmaceutical agent, comprising: mixing a pharmaceutically acceptable additive with bitter taste-masked granules comprising besifovir dipivoxil or a pharmaceutically acceptable salt thereof, coated with a lipid excipient; and forming the mixture into an oral pharmaceutical agent.

In another aspect, the present disclosure refers to a method of preparing a pharmaceutical agent, comprising: mixing a pharmaceutically acceptable additive with bitter taste-masked granules comprising besifovir dipivoxil or a pharmaceutically acceptable salt thereof and being coated with a lipid excipient, wherein the lipid excipient is at least one fatty acid ester selected from the group consisting of glycerol distearate, glyceryl stearate, glyceryl oleate, glyceryl myristate, cetyl palmitate, cetyl caprate, stearyl palmitate, and stearyl stearate; and forming the mixture into an oral pharmaceutical agent.

【Advantageous Effects】

- Granules or pharmaceutical compositions comprising besifovir dipivoxil or a pharmaceutically acceptable salt thereof according to the present disclosure can suppress intrinsic stickiness of the drug, thereby increasing productivity and can effectively mask bitter taste of the drug, thereby improving compliance to administration.
- A preparation method according to the present disclosure can prevent failure in tableting due to stickiness of a drug upon compression molding, thereby allowing continuous compression molding.
- A preparation method according to the present disclosure can eliminate a need to use water or a solvent, thereby preventing decomposition of a drug and thus improving stability of the drug.

【CLAIMS】

【Claim 1】

Bitter taste-masked granules comprising besifovir dipivoxil or a pharmaceutically acceptable salt thereof, and being coated with a lipid excipient, wherein the lipid excipient is at least one fatty acid ester selected from the group consisting of glycerol distearate, glyceryl stearate, glyceryl oleate, glyceryl myristate, cetyl palmitate, cetyl caprate, stearyl palmitate, and stearyl stearate.

【Claim 2】

The bitter taste-masked granules according to claim 1, wherein the lipid excipient is present in an amount of 10 parts by weight to 70 parts by weight relative to 100 parts by weight of the besifovir dipivoxil or the pharmaceutically acceptable salt thereof.

【Claim 3】

The bitter taste-masked granules according to claim 1, wherein the lipid excipient has a melting point of 40°C to 90°C.

【Claim 4】

The bitter taste-masked granules according to claim 1, wherein the lipid excipient is at least one fatty acid ester selected from the group consisting of glycerol distearate, glyceryl stearate, glyceryl oleate, and glyceryl myristate.

【Claim 5】

The bitter taste-masked granules according to claim 1, wherein intrinsic bitter taste of the besifovir dipivoxil or the pharmaceutically acceptable salt thereof is not sensed until more than 10 seconds have elapsed after putting an agent containing the besifovir dipivoxil or the pharmaceutically acceptable salt thereof in the mouth without any beverage or water.

【Claim 6】

A method of preparing bitter taste-masked granules comprising besifovir dipivoxil or

a pharmaceutically acceptable salt thereof, and being coated with a lipid excipient, the method comprising:

melting the lipid excipient through heating to a temperature higher than or equal to a melting point of the lipid excipient, wherein the lipid excipient is at least one fatty acid ester selected from the group consisting of glycerol distearate, glyceryl stearate, glyceryl oleate, glyceryl myristate, cetyl palmitate, cetyl caprate, stearyl palmitate, and stearyl stearate;

mixing the melt with the besifovir dipivoxil or the pharmaceutically acceptable salt thereof in a solid state; and

cooling the mixture.

【Claim 7】

The method according to claim 6, wherein the lipid excipient has a melting point of 40°C to 90°C.

【Claim 8】

The method according to claim 6, wherein cooling the mixture comprises cooling the mixture to a temperature of 10℃ to 40℃.

【Claim 9】

The method according to claim 6, further comprising:

sieving the cooled mixture after cooling the mixture.

【Claim 10】

A pharmaceutical composition comprising:

the bitter taste-masked granules according to any one of claims 1 to 5; and

a pharmaceutically acceptable additive.

【Claim 11】

The pharmaceutical composition according to claim 10, wherein the bitter taste-masked granules are present in an amount of 20 wt% to 70 wt% based on the total weight of the pharmaceutical composition.

【Claim 12】

The pharmaceutical composition according to claim 10, wherein the pharmaceutical composition is a tablet obtained by directly tableting a mixture of the bitter taste-masked granules and the pharmaceutically acceptable additive.

【Claim 13】

A method of preparing a pharmaceutical agent, comprising:

mixing a pharmaceutically acceptable additive with bitter taste-masked granules comprising besifovir dipivoxil or a pharmaceutically acceptable salt thereof and being coated with a lipid excipient, wherein the lipid excipient is at least one fatty acid ester selected from the group consisting of glycerol distearate, glyceryl stearate, glyceryl oleate, glyceryl myristate, cetyl palmitate, cetyl caprate, stearyl palmitate, and stearyl stearate; and

forming the mixture into an oral pharmaceutical agent.

【Claim 14】

The method according to claim 13, wherein the pharmaceutical agent is prepared by directly tableting the mixture.