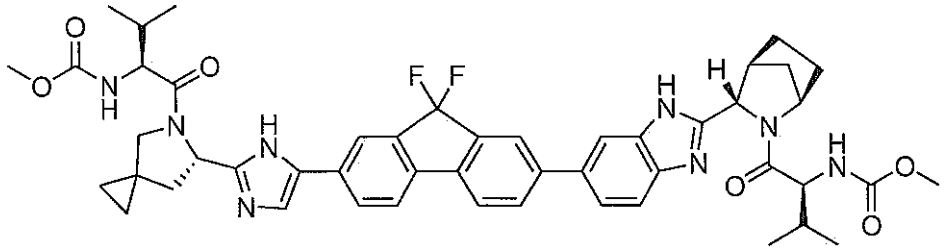
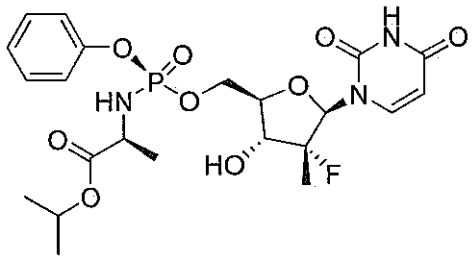
[0006] Ledipasvir has the chemical name of (1-{3-[6-(9,9-difluoro-7-{2-[5-(2-methoxycarbonylamino-3-methyl-butyryl)-5-aza-spiro[2.4]hept-6-yl]-3H-imidazol-4-yl}-9H-fluoren-2-yl)-1H-benzoimidazol-2-yl]-2-aza-bicyclo[2.2.1]heptane-2-carbonyl}-2-methyl-propyl)-carbamic acid methyl ester, and has the following chemical formula:



[0007] Sofosbuvir (SOF) has the chemical name of (S)-isopropyl 2-(((S)-(((2R,3R,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-fluoro-3-hydroxy-4-methyltetrahydrofuran-2-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate and has the following chemical formula:

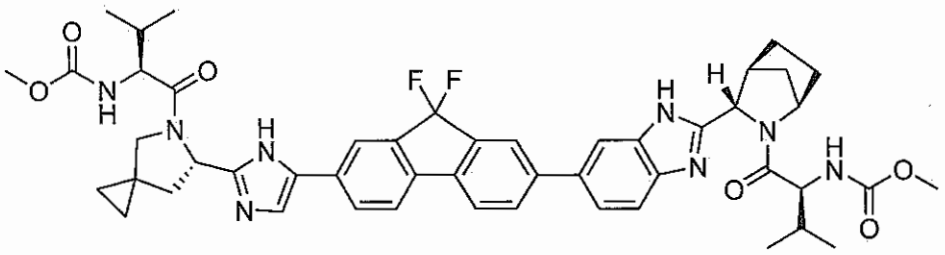


[0008] In some embodiments, provided is a pharmaceutical composition comprising: a) an effective amount of ledipasvir, wherein ledipasvir is substantially amorphous; and b) an effective amount of sofosbuvir wherein sofosbuvir is substantially crystalline.

[0009] Further embodiments of the disclosure relate to pharmaceutical dosage forms and tablets. The disclosure also provides methods for using the combination in the treatment of hepatitis C.

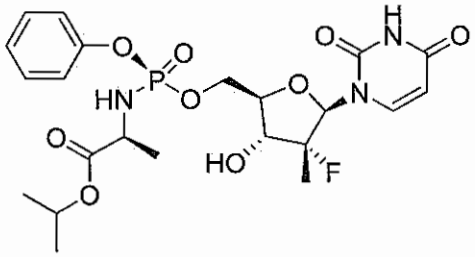
[0009a] In one aspect, there is provided use of a pharmaceutical composition in the preparation of a medicament for treating a patient infected with hepatitis C virus, wherein the composition is in the form of a fixed dose combination tablet comprising:

a) from about 10% to about 25% w/w of a solid dispersion comprising ledipasvir dispersed within a polymer matrix formed by copovidone, wherein the weight ratio of ledipasvir to copovidone in the solid dispersion is about 1:1 and wherein ledipasvir is substantially amorphous and has the formula:



; and

b) from about 35% to about 45% w/w of sofosbuvir, wherein sofosbuvir is substantially crystalline, wherein the crystalline sofosbuvir has XRPD 2θ-reflections (° ± 0.2θ) at about: 6.1 and 12.7 and wherein sofosbuvir has the formula:



;

c) from about 5.0% to about 25% w/w of lactose monohydrate;

d) from about 5.0% to about 25% w/w of microcrystalline cellulose;

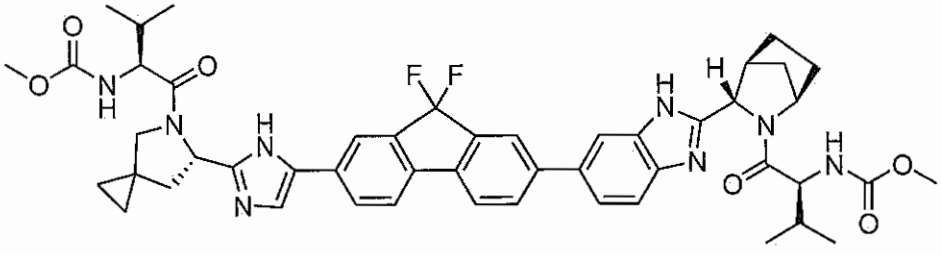
e) from about 1.0% to about 10% w/w of croscarmellose sodium;

f) from about 0.5% to about 3% w/w of colloidal silicon dioxide; and

g) from about 0.1% to about 3% w/w of magnesium stearate.

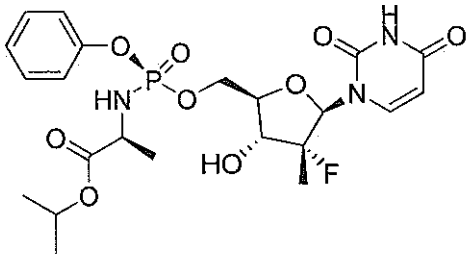
[0009b] In another aspect, there is provided use of a pharmaceutical composition in the preparation of a medicament for treating a patient infected with hepatitis C virus, wherein the composition is in the form of a fixed dose combination tablet comprising:

a) about 18% w/w of a solid dispersion comprising ledipasvir dispersed within a polymer matrix formed by copovidone, wherein the weight ratio of ledipasvir to copovidone in the solid dispersion is about 1:1 and wherein ledipasvir is substantially amorphous and has the formula:



;

b) about 40% w/w of sofosbuvir, wherein sofosbuvir is substantially crystalline, wherein the crystalline sofosbuvir has XRPD 2θ-reflections (° ± 0.2θ) at about: 6.1 and 12.7 and wherein sofosbuvir has the formula:



;

c) about 16.5% w/w of lactose monohydrate;

d) about 18.0% w/w of microcrystalline cellulose;

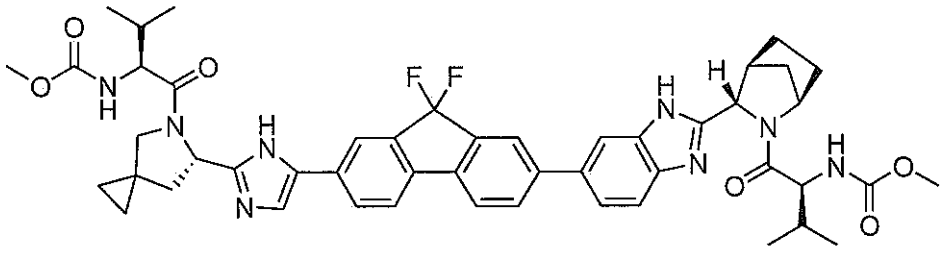
e) about 5.0% w/w of croscarmellose sodium;

f) about 1.0% w/w of colloidal silicon dioxide; and

g) about 1.5% w/w of magnesium stearate.

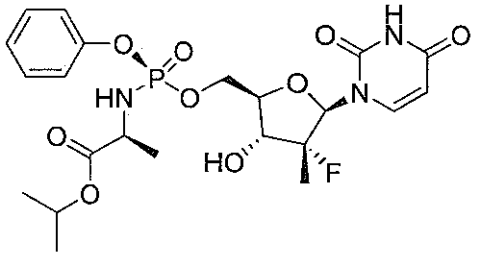
[0009c] In another aspect, there is provided use of a pharmaceutical composition in the preparation of a medicament for treating a patient infected with hepatitis C virus, wherein the composition is in the form of a fixed dose combination tablet comprising:

a) about 180 mg of a solid dispersion comprising ledipasvir dispersed within a polymer matrix formed by copovidone, wherein the weight ratio of ledipasvir to copovidone in the solid dispersion is about 1:1 and wherein ledipasvir is substantially amorphous and has the formula:



;

b) about 400 mg of sofosbuvir, wherein sofosbuvir is substantially crystalline, wherein the crystalline sofosbuvir has XRPD 2θ-reflections (° ± 0.2θ) at about: 6.1 and 12.7 and wherein sofosbuvir has the formula:



;

c) about 165 mg of lactose monohydrate;

d) about 180 mg of microcrystalline cellulose;

e) about 50 mg of croscarmellose sodium;

f) about 10 mg of colloidal silicon dioxide; and

g) about 15 mg of magnesium stearate.

BRIEF DESCRIPTION OF THE DRAWINGS

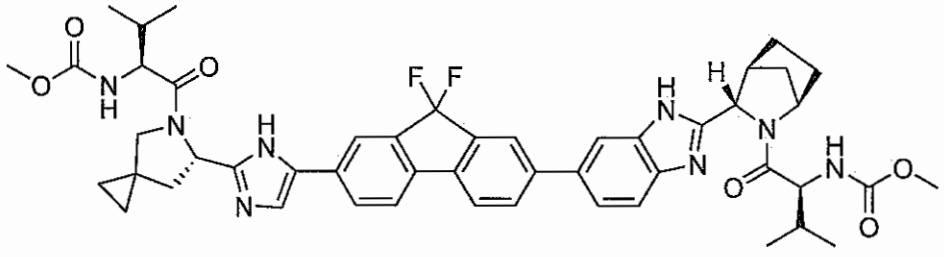
[0010] **FIG. 1** is a XRPD pattern of the solid dispersion formulation of ledipasvir comprising copovidone in a drug:polymer ratio of 1:1. As shown by the XRPD, the solid dispersion is in the amorphous state.

[0011] **FIG. 2** is a modulated differential scanning calorimetry (DSC) curve of the solid dispersion of ledipasvir comprising copovidone in a drug:polymer ratio of 1:1. The glass transition temperature of the solid dispersion is about 140 °C.

WE CLAIM:

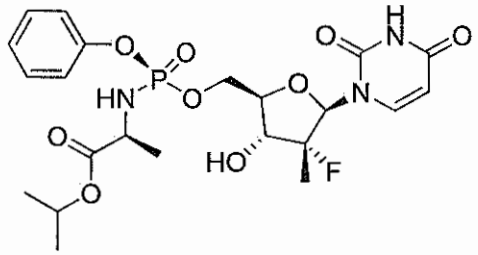
1. Use of a pharmaceutical composition in the preparation of a medicament for treating a patient infected with hepatitis C virus, wherein the composition is in the form of a fixed dose combination tablet comprising:

a) from about 10% to about 25% w/w of a solid dispersion comprising ledipasvir dispersed within a polymer matrix formed by copovidone, wherein the weight ratio of ledipasvir to copovidone in the solid dispersion is about 1:1 and wherein ledipasvir is substantially amorphous and has the formula:



; and

b) from about 35% to about 45% w/w of sofosbuvir, wherein sofosbuvir is substantially crystalline, wherein the crystalline sofosbuvir has XRPD 2θ-reflections (° ± 0.2θ) at about: 6.1 and 12.7 and wherein sofosbuvir has the formula:



;

c) from about 5.0% to about 25% w/w of lactose monohydrate;

d) from about 5.0% to about 25% w/w of microcrystalline cellulose;

e) from about 1.0% to about 10% w/w of croscarmellose sodium;

f) from about 0.5% to about 3% w/w of colloidal silicon dioxide; and

g) from about 0.1% to about 3% w/w of magnesium stearate.

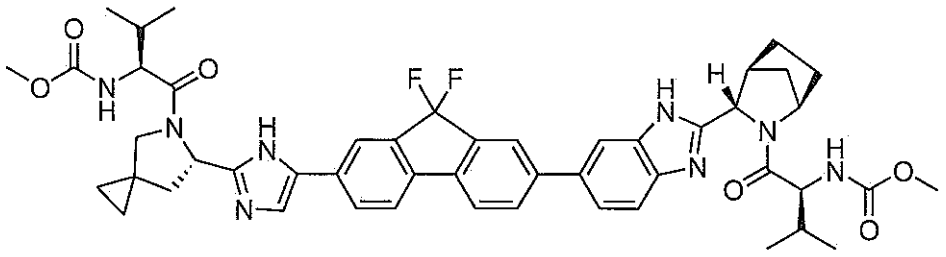
2. The use according to claim 1, wherein the pharmaceutical composition comprises about 40% w/w of sofosbuvir.

3. The use according to claim 1 or 2 wherein the pharmaceutical composition comprises about 18 %w/w of the solid dispersion.

4. The use according to claim 1 wherein the pharmaceutical composition has from about 50 mg to about 130 mg of ledipasvir and from about 300 mg to about 600mg of sofosbuvir.

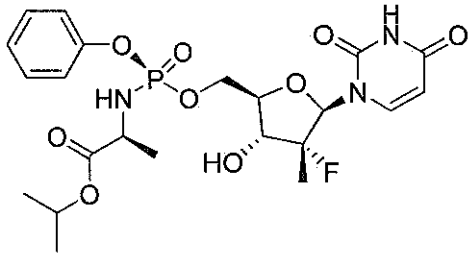
5. Use of a pharmaceutical composition in the preparation of a medicament for treating a patient infected with hepatitis C virus, wherein the composition is in the form of a fixed dose combination tablet comprising:

a) about 18% w/w of a solid dispersion comprising ledipasvir dispersed within a polymer matrix formed by copovidone, wherein the weight ratio of ledipasvir to copovidone in the solid dispersion is about 1:1 and wherein ledipasvir is substantially amorphous and has the formula:



;

b) about 40% w/w of sofosbuvir, wherein sofosbuvir is substantially crystalline, wherein the crystalline sofosbuvir has XRPD 2θ-reflections (° ± 0.2θ) at about: 6.1 and 12.7 and wherein sofosbuvir has the formula:



;

c) about 16.5% w/w of lactose monohydrate;

d) about 18.0% w/w of microcrystalline cellulose;

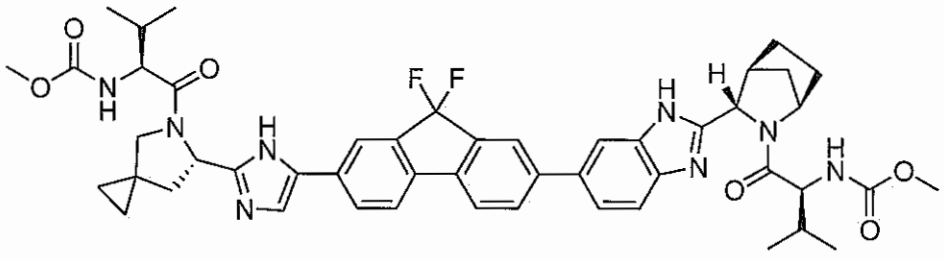
e) about 5.0% w/w of croscarmellose sodium;

f) about 1.0% w/w of colloidal silicon dioxide; and

g) about 1.5% w/w of magnesium stearate.

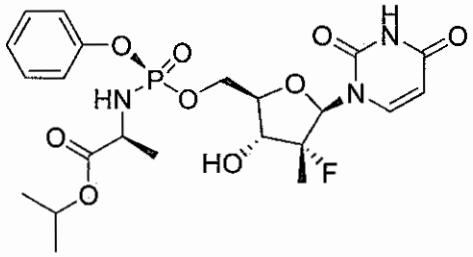
6. Use of a pharmaceutical composition in the preparation of a medicament for treating a patient infected with hepatitis C virus, wherein the composition is in the form of a fixed dose combination tablet comprising:

a) about 180 mg of a solid dispersion comprising ledipasvir dispersed within a polymer matrix formed by copovidone, wherein the weight ratio of ledipasvir to copovidone in the solid dispersion is about 1:1 and wherein ledipasvir is substantially amorphous and has the formula:



;

b) about 400 mg of sofosbuvir, wherein sofosbuvir is substantially crystalline, wherein the crystalline sofosbuvir has XRPD 2θ-reflections (° ± 0.2θ) at about: 6.1 and 12.7 and wherein sofosbuvir has the formula:



;

c) about 165 mg of lactose monohydrate;

d) about 180 mg of microcrystalline cellulose;

e) about 50 mg of croscarmellose sodium;

f) about 10 mg of colloidal silicon dioxide; and

g) about 15 mg of magnesium stearate.

7. The use according to any one of claims 1 to 6 wherein the pharmaceutical composition further comprises a film coating.