

It is still further another object of the present invention to provide the use of a peptide including any one of the amino acid sequences of SEQ ID NOS: 20, 22, 33, 37, and 38 or a conjugate including the same, or a composition including the same in the preparation of a medicament for preventing or treating liver disease.

It is still further another object of the present invention to provide the use of a peptide including any one of the amino acid sequences of SEQ ID NOS: 20, 22, 33, 37, and 38 or a conjugate including the same, or a composition including the same in the prevention or treatment of liver disease.

[Advantageous Effects]

The peptide having activity on the glucagon receptor according to the present invention or a conjugate thereof can be effectively used for preventing or treating liver disease.

[Summary]

In one aspect, the present disclosure relates to use of a pharmaceutical composition in the manufacture of a medicament for preventing or treating liver disease, wherein the pharmaceutical composition comprises a pharmaceutically acceptable excipient; and a peptide comprising the amino acid sequence of General Formula 1 below in a pharmaceutically effective amount: Y-X2-QGTF-X7-SDYSKY-X14-D-X16-X17-R-X19-X20-X21-FVQWLMNT-X30 (General Formula 1, SEQ ID NO: 46) wherein, X2 is aminoisobutyric acid (Aib); X7 is threonine (T), valine (V), or cysteine (C); X14 is leucine (L) or cysteine (C); X16 is glutamic acid (E) or serine (S); X17 is lysine (K), arginine (R), or cysteine (C); X19 is alanine (A) or cysteine (C); X20 is lysine (K) or glutamine (Q); X21 is aspartic acid (D) or glutamic acid (E); and X30 is cysteine (C) or is absent (with the proviso that when the amino acid sequence of General Formula 1 is identical to SEQ ID NO: 1 or SEQ ID NO: 12, it is excluded).

In another aspect, the present disclosure related to use of a pharmaceutical composition in the manufacture of a medicament for preventing or treating liver disease, comprising a pharmaceutically acceptable excipient; and a peptide

comprising any one of amino acid sequences of SEQ ID NOS: 20, 22, 33, 37, and 38.

[Brief Description of Drawings]

FIG. 1 is a diagram confirming the effect of the long-acting conjugate of the glucagon derivative of SEQ ID NO: 37 according to the present invention on hepatitis.

FIG. 2 is a diagram confirming the effect of the long-acting conjugate of the glucagon derivative of SEQ ID NO: 37 according to the present invention on liver fibrosis.

FIG. 3 is a diagram confirming the effect of the long-acting conjugate of the glucagon derivative of SEQ ID NO: 37 on reducing triglyceride in the liver according to the present invention.

[Detailed Description of the Invention]

One aspect for implementing the present invention provides a composition including a peptide or a conjugate including the peptide, specifically a pharmaceutical composition for preventing or treating liver disease.

In one embodiment, the present invention relates to a pharmaceutical composition for preventing or treating liver disease, including a pharmaceutically

[CLAIMS]

[Claim 1]

Use of Aa pharmaceutical composition in the manufacture of a medicament for preventing or treating liver disease, ~~comprising wherein the pharmaceutical composition comprises~~ a pharmaceutically acceptable excipient; and a peptide comprising the amino acid sequence of General Formula 1 below in a pharmaceutically effective amount:

Y-X2-QGTF-X7-SDYSKY-X14-D-X16-X17-R-X19-X20-X21-FVQWLMNT-X30

(General Formula 1, SEQ ID NO: 46)

wherein,

X2 is aminoisobutyric acid (Aib);

X7 is threonine (T), valine (V), or cysteine (C);

X14 is leucine (L) or cysteine (C);

X16 is glutamic acid (E) or serine (S);

X17 is lysine (K), arginine (R), or cysteine (C);

X19 is alanine (A) or cysteine (C);

X20 is lysine (K) or glutamine (Q);

X21 is aspartic acid (D) or glutamic acid (E); and

X30 is cysteine (C) or is absent (with the proviso that when the amino acid sequence of General Formula 1 is identical to SEQ ID NO: 1 or SEQ ID NO: 12, it is excluded).

[Claim 2]

~~The pharmaceutical composition~~use of claim 1, wherein the peptide is in the form of a long-acting conjugate, and the long-acting conjugate is represented by Chemical Formula 1 below:

[Chemical Formula 1]

X–L–F

with the proviso that X is a peptide comprising the amino acid sequence of General Formula 1 above;

L is a linker containing ethylene glycol repeating units;

F is an immunoglobulin Fc region; and

– represents a covalent bond between X and L, and L and F.

[Claim 3]

The ~~use~~pharmaceutical composition of claim 1 or 2, wherein the liver disease is any one selected from the group consisting of steatosis, liver fibrosis, liver inflammation, liver cirrhosis, liver decompensation, hepatocellular carcinoma, and cholestasis liver disease.

[Claim 4]

The ~~use~~pharmaceutical composition of claim 3, wherein the cholestasis liver disease is any one selected from the group consisting of primary biliary cirrhosis, primary sclerosing cholangitis, and a combination thereof.

[Claim 5]

The ~~use~~pharmaceutical composition of claim 3, wherein the liver disease is caused by non-alcoholic steatohepatitis (NASH) or is accompanied thereby.

[Claim 6]

The ~~use~~pharmaceutical composition of claim 1 or 2, wherein the peptide comprises an amino acid sequence selected from SEQ ID NOS: 20, 22, 23, 27, 33, 35, 37, 38, 40, 41, 42, and 44.

[Claim 7]

The ~~use~~pharmaceutical composition of claim 1 or 2, wherein the peptide comprises an amino acid sequence selected from SEQ ID NOS: 20, 22, 23, 27, 33, 37, 38, and 44.

[Claim 8]

The ~~use~~pharmaceutical composition of claim 1 or 2, wherein the pharmaceutical composition reduces a liver inflammation score in the administered subject upon administration.

[Claim 9]

The ~~use~~pharmaceutical composition of claim 1 or 2, wherein the

pharmaceutical composition reduces hydroxyproline content in the administered subject upon administration.

[Claim 10]

The ~~use~~pharmaceutical composition of claim 1 or 2, wherein the pharmaceutical composition reduces triglyceride content in the liver tissue in the administered subject upon administration.

[Claim 11]

The ~~use~~pharmaceutical composition of claim 1 or 2, wherein the C-terminus of the peptide is amidated.

[Claim 12]

The ~~use~~pharmaceutical composition of claim 2, wherein the formula weight of the ethylene glycol repeating unit moiety in L is in the range of 1 kDa to 100 kDa.

[Claim 13]

Use of Aa pharmaceutical composition in the manufacture of a medicament for preventing or treating liver disease, comprising a pharmaceutically acceptable excipient; and

a peptide comprising any one of amino acid sequences of SEQ ID NOS: 20, 22, 33, 37, and 38.

[Claim 14]

The ~~use~~pharmaceutical composition of claim 13, wherein the peptide is in the form of a long-acting conjugate, and the long-acting conjugate is represented by Chemical Formula 1 below:

[Chemical Formula 1]

X–L–F

with the proviso that X is a peptide comprising any one of amino acid sequences of SEQ ID NOS: 20, 22, 33, 37, and 38;

L is a linker containing ethylene glycol repeating units;

F is an immunoglobulin Fc region; and

– represents a covalent bond between X and L, and L and F.

[Claim 15]

The ~~use~~pharmaceutical composition of claim 13 or 14, wherein the liver disease is any one selected from the group consisting of steatosis, liver fibrosis, liver inflammation, liver cirrhosis, liver decompensation, hepatocellular carcinoma, and cholestasis liver disease.

[Claim 16]

The ~~use~~pharmaceutical composition of claim 15, wherein the cholestasis liver disease is any one selected from the group consisting of primary biliary cirrhosis, primary sclerosing cholangitis, and a combination thereof.

[Claim 17]

The ~~use~~pharmaceutical composition of claim 15, wherein the liver disease is caused by non-alcoholic steatohepatitis (NASH) or is accompanied thereby.