

CLAIMS

1. Use of a pharmaceutical composition in the manufacture of a medicament for the prevention or treatment of mucositis induced by radiotherapy, chemotherapy, or a combination thereof, the pharmaceutical composition comprising:

a pharmaceutically acceptable excipient; and

a glucagon-like peptide-2 (GLP-2) derivative in a pharmaceutically effective amount, wherein the GLP-2 derivative comprises an amino acid sequence represented by General Formula 1 below:

[General Formula 1]

$X_1X_2DGSFSDEMNTILDNLAARDFINWLIQTX_{30}ITDX_{34}$ (SEQ ID NO: 10)

wherein

X_1 is histidine, imidazoacetyldeshistidine, desaminohistidine, β -hydroxyimidazopropionyl-deshistidine, *N*-dimethylhistidine, or β -carboxyimidazopropionyl-deshistidine;

X_2 is alanine, glycine, or 2-aminoisobutyric acid (Aib);

X_{30} is lysine or arginine;

X_{34} is at least one amino acid or at least one altered amino acid; and

with the proviso that a sequence identical to SEQ ID NO: 1 is excluded from the amino acid sequence of General Formula 1.

2. The use of to claim 1, wherein the GLP-2

derivative comprises an amino acid sequence represented by General Formula 2 below:

[General Formula 2]

$X_1X_2DGSFSDEMNTILDNLAARDFINWLIQTX_{30}ITDX_{34}$ (SEQ ID NO: 9)

wherein

X_1 is histidine, imidazoacetyldeshistidine, desaminohistidine, β -hydroxyimidazopropionyl-deshistidine, *N*-dimethylhistidine, or β -carboxyimidazopropionyl-deshistidine;

X_2 is alanine, glycine, or 2-aminoisobutyric acid (Aib);

X_{30} is lysine or arginine;

X_{34} is absent, or lysine, arginine, glutamine, histidine, 6-azidolysine, or cysteine; and

with the proviso that a sequence identical to SEQ ID NO: 1 is excluded from the amino acid sequence of General Formula 2.

3. The use of claim 2, wherein in the GLP-2 derivative,

(1) X_1 is imidazoacetyldeshistidine, X_2 is glycine, X_{30} is lysine, and X_{34} is cysteine,

(2) X_1 is imidazoacetyldeshistidine, X_2 is glycine, X_{30} is lysine, and X_{34} is lysine,

(3) X₁ is imidazoacetyldeshistidine, X₂ is glycine, X₃₀ is arginine, and X₃₄ is lysine,

(4) X₁ is imidazoacetyldeshistidine, X₂ is glycine, X₃₀ is lysine, and X₃₄ is 6-azidolysine,

(5) X₁ is imidazoacetyldeshistidine, X₂ is glycine, X₃₀ is arginine, and X₃₄ is cysteine,

(6) X₁ is imidazoacetyldeshistidine, X₂ is Aib, X₃₀ is lysine, and X₃₄ is cysteine,
or

(7) X₁ is histidine, X₂ is Aib, X₃₀ is lysine, and X₃₄ is cysteine.

4. The use of claim 1, wherein the GLP-2 derivative comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 2 to 8.

5. The use of claim 1, wherein a C-terminus of the GLP-2 derivative is non-altered or amidated.

6. The use of claim 1, wherein the mucositis is oral mucositis, gastrointestinal mucositis, or a combination thereof.

7. The use of claim 1, wherein the chemotherapy is chemotherapy using an anticancer drug.

8. The use of claim 7, wherein the anticancer drug is a cytotoxic anticancer agent, a targeted anticancer agent, an immunooncology agent, or a combination thereof.

9. The use of claim 8, wherein the cytotoxic anticancer agent is a nucleoside analogue, an antifolate, an antimetabolite, a topoisomerase I inhibitor, an anthracycline, a podophyllotoxin, a taxane, a vinca alkaloid, an alkylating agent, a platinum compound, or a combination thereof.

10. The use of claim 7, wherein the anticancer drug is 5-fluorouracil (5-FU), cyclophosphamide (CPA), Docetaxel, Doxorubicin, Vincristine, Prednisone, Etoposide, ifosfamide, Methotrexate, Paclitaxel, Gemcitabine, Vinorelbine, Leucovorin, Irinotecan, Oxaliplatin, or a combination thereof.

11. The use of claim 1, wherein the medicament is to be administered within 1 day before conducting radiotherapy or chemotherapy; or within 1 day after conducting radiotherapy or chemotherapy.

12. The use of claim 1, wherein administration of the medicament leads to at least one of an increase in small intestine mass, a decrease in a small intestine mass reduction level,

an inhibition of inflammation, an inhibition of differentiation of monocytes into macrophages, and an inhibition of migration of monocytes, in a subject administered with the composition.

13. The use of any one of claims 1 to 12, wherein the GLP-2 derivative is in the form of a long-acting conjugate in which the GLP-2 derivative is linked to a biocompatible material capable of increasing an *in vivo* half-life of the GLP-2 derivative.

14. The use of claim 13, wherein the conjugate is represented by Chemical Formula 1 below:

[Chemical Formula 1]

X-La-F

wherein,

X is a GLP-2 derivative;

L is a linker comprising an ethyleneglycol repeating unit;

a is 0 or a natural number with the proviso that when a is 2 or more, each L is independent of the other;

F is an immunoglobulin Fc region; and

the “-” is a covalent bond.

15. The use of claim 14, wherein the immunoglobulin Fc region is an aglycosylated IgG4 Fc region.

16. The use of claim 14, wherein the F is a dimer consisting of two polypeptide chains, and one end of the L is linked to only one polypeptide chain of the two polypeptide chains.

17. The use of claim 14, wherein the L is polyethylene glycol.

18. The use of claim 14, wherein a formula weight of the ethyleneglycol repeating unit moiety in the L is in a range of 1 kDa to 100 kDa.