

the contents of GLP-1 and glucagon may be more effective.

However, for the combined therapy, it is required to improve the physical characteristics of glucagon, which aggregates at a neutral pH and precipitates with time, thus showing poor solubility.

Under these circumstances, the present inventors have developed glucagon derivatives with partial modifications of the amino acid sequence of glucagon for the improvement of the therapeutic effects of glucagon on hypoglycemia and obesity by improving the physical properties of glucagon, and have discovered that these glucagon derivatives have improved solubility and higher stability at a neutral pH, thereby completing the present invention.

[Disclosure]

[Technical Problem]

An object of the present invention is to provide a novel glucagon derivative with improved physical properties.

Another object of the present invention is to provide a composition for preventing or treating hypoglycemia containing the glucagon derivative as an active ingredient.

A further object of the present invention is to provide a composition for preventing or treating obesity containing the glucagon derivative as an active ingredient.

[Technical Solution]

In order to achieve the above objects, in an aspect, the present invention provides a novel glucagon derivative as defined in the appending claim set. In one aspect, the present disclosure refers to a glucagon derivative, which comprises the amino acid sequence selected from the group consisting of amino acid sequences represented by SEQ ID NOS: 2 to 11, and 14 to 34. Also disclosed herein is a glucagon derivative which includes the amino acid sequence of the following General Formula 1 and has an isoelectric point (pI), which is not the same as, i.e., different from, that of native glucagon:

X1-X2-QGTF-X7-SDYS-X12-X13-X14-X15-X16-X17-X18-X19-X20-X21-F-X23-X24-W-L-X27-X28-T (General Formula 1)

wherein, in General Formula 1,

X1 is histidine, desamino-histidine, N-dimethyl-histidine, β -hydroxyimidazopropionic acid, 4-imidazoacetic acid, β -carboxyimidazopropionic acid, tryptophan, tyrosine, or deleted;

[CLAIMS]

[Claim 1]

A glucagon derivative, which comprises the amino acid sequence selected from the group consisting of amino acid sequences represented by SEQ ID NOS: 2 to 11, and 14 to 34.

[Claim 2]

A polynucleotide encoding the glucagon derivative of claim 1.

[Claim 3]

Use of a glucagon derivative of claim 1 as an active ingredient in the manufacture of a pharmaceutical composition for preventing or treating hypoglycemia.

[Claim 4]

Use of a glucagon derivative of claim 1 as an active ingredient in the manufacture of a pharmaceutical composition for preventing or treating obesity.

[Claim 5]

The use according to claim 3, further comprising a pharmaceutically acceptable carrier.

[Claim 6]

The use according to claim 4, further comprising a pharmaceutically acceptable carrier.

[Claim 7]

The use according to claim 4, wherein the pharmaceutical composition is to be administered alone or in combination with a pharmaceutical agent having the effect of preventing or treating obesity.

[Claim 8]

The use according to claim 4, further comprising a pharmaceutical agent having the effect of preventing or treating obesity.

[Claim 9]

The use according to claim 7, wherein the pharmaceutical agent having the effect of preventing or treating obesity is selected from the group consisting of a GLP-1 receptor agonist, a glucose-dependent insulintropic peptide (GIP) receptor antagonist, a leptin receptor agonist, a DPP-IV inhibitor, a Y5 receptor antagonist, a melanin-concentrating hormone (MCH) receptor antagonist, a Y2/3/4 receptor agonist, an MC3/4 receptor agonist, a gastric/pancreatic lipase inhibitor, a 5HT2c agonist, a β 3A receptor agonist, an amylin receptor agonist, a ghrelin antagonist, a ghrelin receptor antagonist, FGF1, an FGF21 receptor agonist, a cholecystokinin (CCK) receptor agonist, a pancreatic polypeptide (PP) receptor agonist, a dopamine reabsorption inhibitor, and a combination thereof.

[Claim 10]

The use according to claim 8, wherein the pharmaceutical agent having the effect of preventing or treating obesity is selected from the group consisting of a GLP-1 receptor agonist, a glucose-dependent insulintropic peptide (GIP) receptor antagonist, a leptin receptor agonist, a DPP-IV inhibitor, a Y5 receptor antagonist, a melanin-concentrating hormone (MCH) receptor antagonist, a Y2/3/4 receptor agonist, an MC3/4 receptor agonist, a gastric/pancreatic lipase inhibitor, a 5HT2c agonist, a β 3A receptor agonist, an amylin receptor agonist, a ghrelin antagonist, a ghrelin receptor antagonist, FGF1, an FGF21 receptor agonist, a cholecystokinin (CCK) receptor agonist, a pancreatic polypeptide (PP) receptor agonist, a dopamine reabsorption inhibitor, and a combination thereof.

[Claim 11]

A glucagon derivative of claim 1, or a pharmaceutical composition containing the same for use in therapy.

GLUCAGON DERIVATIVE HAVING IMPROVED STABILITY

[ABSTRACT]

The present invention relates to a novel glucagon derivative peptide, and a composition for preventing or treating hypoglycemia containing the novel glucagon derivative peptide as an active ingredient. The glucagon derivative according to the present invention has improved physical properties due to the change in isoelectric point (pI) while being capable of maintaining an activity on glucagon receptors, and thus can improve patient compliance when used as a hypoglycemic agent, and is also suitable for administration in combination with other anti-obesity agents. Accordingly, the glucagon derivative according to the present invention can be effectively used for the prevention and treatment of hypoglycemia and obesity.

[No suitable figure]