Description

Pharmaceutical Composition for Treating a Metabolic Syndrome

The present invention is directed to a pharmaceutical composition containing at least one FGF-21 (fibroblast growth factor 21) compound, at least one GLP-1R (glucagon-like peptide-1 receptor) agonist and optionally at least one anti-diabetic drug and/or at least one DPP-4 (dipeptidyl peptidase-4) inhibitor for the treatment of at least one metabolic syndrome and/or atherosclerosis, in particular diabetes, dyslipidemia, obesity and/or adipositas.

In one aspect, there is provided use of a pharmaceutical composition containing at least one FGF-21 (fibroblast growth factor 21) compound and at least one GLP-1R (glucagon-like peptide-1 receptor) agonist for the preparation of a medicament for treating diabetes in a patient, wherein the pharmaceutical composition further comprises an acceptable pharmaceutical carrier, diluent or excipient selected from the group consisting of sterile water, saline containing about 0.9% mg/ml benzyl alcohol, Hank's solution, Ringer's-lactate, lactose, dextrose, sucrose, trehalose, sorbitol, and mannitol.

Diabetes mellitus is characterized by its clinical manifestations, namely the non-insulin-dependent or maturity onset form, also known as Type 2 diabetes and the insulin-dependent or juvenile onset form, also known as Type 1 diabetes. The manifestations of clinical symptoms of Type 2 diabetes and the underlying obesity usually appear at an age over 40. In contrast, Type 1 diabetes usually shows a rapid onset of the disease often before 30. The disease is a metabolic disorder in humans with a prevalence of approximately one percent in the general population, with one-fourth of these being Type 1 and three-fourth of these being Type 2 diabetes. Type 2 diabetes is a disease characterized by high-circulating blood glucose, insulin and corticosteroid levels.

Currently, there are various pharmacological approaches for the treatment of Type 2 diabetes, which may be utilized individually or in combination, and which act via different modes of action:
1) sulfonylurea stimulate insulin secretion;
2) biguanides (metformin) act by promoting glucose utilization, reducing hepatic glucose production and diminishing intestinal glucose output;
3) oc-glucosidase inhibitors (acarbose, miglitol) slow down carbohydrate digestion and consequently absorption from the gut and reduce postprandial hyperglycemia;
4) thiazolidinediones (troglitazone) enhance insulin action, thus promoting glucose utilization in peripheral tissues; and
5) insulin stimulates tissue glucose utilization and inhibits hepatic glucose output.

However, most of the drugs have limited efficacy and do not address the most important problems, the declining β-cell function and the associated obesity.
Obesity is a chronic disease that is highly prevalent in modern society and is associated with numerous medical problems including diabetes mellitus, insulin resistance, hypertension, hypercholesterolemia, and coronary heart disease. It is further highly correlated with diabetes and insulin resistance, the latter of which is generally

Claims

1. Use of a pharmaceutical composition containing at least one FGF-21 (fibroblast growth factor 21) compound and at least one GLP-1R (glucagon-like peptide-1 receptor) agonist for the preparation of a medicament for treating diabetes in a patient, wherein the pharmaceutical composition further comprises an acceptable pharmaceutical carrier, diluent or excipient selected from the group consisting of sterile water, saline containing about 0.9% mg/ml benzyl alcohol, Hank's solution, Ringer's-lactate, lactose, dextrose, sucrose, trehalose, sorbitol, and mannitol.

2. The use of claim 1, wherein the composition further contains at least one anti-diabetic drug and/or at least one DPP-4 (dipeptidyl peptidase-4) inhibitor.

3. The use of claim 1 or 2, wherein the FGF-21 compound(s), the GLP-1 R agonist(s), optionally the anti-diabetic drug(s) and optionally the DPP-4 inhibitor are combined in one formulation or contained in several formulations.

4. The use of claim 3, wherein the formulations of the FGF-21 compound(s), the GLP-1 R agonist(s), optionally the anti-diabetic drug(s) and optionally the DPP-4 inhibitor are suitable for simultaneous or subsequent administration(s).

5. The use of at least one of the claims 1-4, wherein the FGF-21 compound is selected from FGF-21 or a FGF-21 mimetic.

6. The use of claim 5, wherein the FGF-21 mimetic is selected from a protein having at least about 96% amino acid sequence identity to the amino acid sequence shown in SEQ ID NO: 1 and having FGF-21 activity, a FGF-21 fusion protein and/or a FGF-21 conjugate.

7. The use of claim 6, wherein the FGF-21 mimetic is selected from a FGF-21 mutein, a FGF-21-Fc fusion protein, a FGF-21-HSA fusion protein and/or a PEGylated FGF-21.

8. The use of at least one of the claims 1-7, wherein the GLP-1 R agonist is selected from a bioactive GLP-1, a GLP-1 analog or a GLP-1 substitute.

9. The use of claim 8, wherein the GLP-1 R agonist is selected from GLP-1 (7-37), GLP-1 (7-36)amide, exendin-4, liraglutide, CJC-1131, albugon, albiglutide, exenatide, exenatide-LAR, oxyntomodulin, lixisenatide, geniproside, a short peptide with GLP-1 R agonistic activity and/or a small organic compound with GLP-1 R agonistic activity.

10. The use of at least one of the claims 2-9, wherein the anti- diabetic drug is selected from metformin, a thiazolidinedione, a sulphonylurea, and/or insulin.

11. The use of at least one of the claims 2-10, wherein the DPP-4 inhibitor is selected from sitagliptin, vildagliptin, saxagliptin, linagliptin, adogliptin and/or berberine.

12. The use of at least one of the claims 1-11, wherein the diabetes is Type 2-diabetes.

13. The use of at least one of the claims 1-12, wherein the patient is selected from a Type 1-diabetic patient, a Type 2-diabetic patient, in particular a diet-treated Type 2-diabetic patient, a sulfonylurea-treated Type 2-diabetic patient, a far-advanced stage Type 2-diabetic patient and/or a long-term insulin-treated Type 2-diabetic patient.