SOLID COMPOSITIONS COMPRISING A GLP-1 AGONIST AND A SALT OF N-(8-(2-HYDROXYBENZOYL)AMINO)CAPRYLIC ACID

TECHNICAL FIELD OF THE INVENTION

The present invention relates to solid compositions comprising a GLP-1 agonist and a salt of N-(8-(2-hydroxybenzoyl)amino)caprylic acid, their method of preparation and their use in medicine.

INCORPORATION-BY-REFERENCE OF THE SEQUENCE LISTING

The Sequence Listing, entitled "SEQUENCE LISTING", is 4 KB and was created April 25th, 2019 and is incorporated herein by reference.

BACKGROUND

Human GLP-1 and analogues thereof have a low oral bioavailability. Exposure and bioavailability of human GLP-1 and analogues thereof is very low following oral administration. Human GLP-1 and analogues thereof can only reach therapeutically relevant plasma concentration after oral administration if formulated with certain absorption enhancers in a specific amount.

Steinert et al. (Am J Clin Nutr, Oct 2010; 92: 810 – 817) discloses oral administration of a tablet comprising GLP-1(7-36)amide and 150 mg sodium N-(8-(2-hydroxybenzoyl)amino)caprylate (SNAC).

WO 2010/020978 discloses an oral pharmaceutical composition comprising a protein and N-(8-[2-hydroxybenzoyl) amino)caprylate (SNAC). Patent applications disclosing oral dosage forms of GLP-1 analogues containing a salt of N-(8-(2-hydroxybenzoyl)amino)caprylate include WO2012/080471, WO2013/189988, WO2013/139694, WO2013/139695 and WO2014/177683.

Despite these findings there is still room for a further optimized pharmaceutical composition for oral administration of a GLP-1 agonist such as a GLP-1 analogue comprising a substituent.

SUMMARY

The present disclosure in an example relates to a composition comprising a GLP-1 agonist, an absorption enhancer or delivery agent and a hydrotrope. The composition according to the disclosure comprises balanced amounts of the delivery agent and the

hydrotrope. The provided compositions display an accelerated absorption, enabling fast and efficient uptake of the active pharmaceutical ingredient.

Oral administration of therapeutic peptides is challenging, due to the rapid degradation of such peptides in the gastrointestinal system.

Described herein are pharmaceutical compositions providing accelerate absorption of the GLP-1 agonist within 15-30 minutes after administration and thereby improved exposure of the GLP-1 agonist by oral administration. The inventors have surprisingly found that an increased exposure of GLP-1 agonists is observed when compositions are prepared with a hydrotrope.

An aspect of the disclosure relates to a composition comprising

i) a GLP-1 agonist,
ii) a salt of N-(8-(2-hydroxybenzoyl)amino)caprylic acid (NAC) and
iii) a hydrotrope,
wherein the hydrotrope is capable of increasing the solubility of SNAC at least 2-fold, such as 5-fold or such as at least 10-fold.

In one example the composition comprises:

i) 0.1-50 mg GLP-1 agonist, such as Semaglutide, GLP-1 agonist B or GLP-1 agonist C.
ii) 50-600 mg salt of N-(8-(2-hydroxybenzoyl)amino)caprylic acid (NAC), such as the sodium salt of NAC (SNAC) and
iii) 20-200 mg nicotinamide or resorcinol and
iv) 0-10 mg lubricant.

A further aspect relates to a method for producing a solid pharmaceutical composition comprising the steps of;

i) obtaining a blend comprising a salt of NAC and a hydrotrope,
ii) co-processing the blend of i) and
iii) preparing said solid pharmaceutical composition using the product of ii).

A further aspect relates to a method of producing a solid pharmaceutical composition comprising the steps of;

i) obtaining a blend comprising a salt of NAC and a hydrotrope,
ii) heat melt extruding the blend of i),
iii) milling the extrudate of ii) and
iv) preparing said solid pharmaceutical composition using the product of iii).

A further aspect relates to a method of producing a solid pharmaceutical composition comprising the steps of

v) obtaining a blend comprising a salt of NAC and a hydrotrope,

vi) heat melt extruding the blend of i),

vii) admixing the extrudate of ii) with an active pharmaceutical ingredient and optionally any further excipients and

viii) preparing said solid pharmaceutical composition using the mixture of iii).

A further example relates to the medical use of compositions described herein. An example relates to pharmaceutical use of compositions described herein, such as compositions for oral administration. In a further example the composition is a pharmaceutical composition for use in a method of treating diabetes and/or obesity.

In a further example the disclosure relates to a method of treating diabetes or obesity comprising administering the composition as defined herein to a patient in need thereof.