Claims

1. A pharmaceutical composition comprising multiple dosage forms each comprising a core and an enteric coating, wherein the core comprises at least one compound stimulating enteroendocrine cells to release at least one enterokine, wherein the size of the dosage forms, with respect to the largest dimension of the dosage forms, provides for entry of the dosage forms into the intestine of a subject independent of gastric emptying mechanisms, ~~and~~ wherein the composition further comprises a gelling composition containing one or more gelling agents, and wherein the multiple dosage forms and the gelling composition form a heterogenous mixture.

2. The composition of claim 1~~according to any one of the preceding claims~~ wherein the size of each of the dosage forms, with respect to the largest dimension of the dosage forms, is below 3 mm, preferably from 0,6 mm to 2,6 mm, more preferably from 0,6 mm to 1,7 mm, even more preferred from 0,8 mm to 1,2 mm.

3. The composition of claim 2 containing 10000 to 40000 dosage forms, preferably 20000 to 30000 dosage forms.

~~4. The composition of claim 3 containing 20000 to 30000 dosage forms.~~

4~~5~~. The composition according to any one of the preceding claims wherein the enteric coating comprises a pH sensitive polymer being selected such that the coating substantially dissolves and/or is substantially degraded in the, preferably terminal, jejunum of a subject such that the core is released into the jejunum, preferably the terminal ~~-~~jejunum, of the subject.

5~~6~~. The composition of claim 4~~5~~ wherein the pH sensitive polymer substantially degrades and/or dissolves at a pH value of ~~about~~ 5.5 to ~~about~~ 7.5, preferably ~~about~~ 7.2 to ~~about~~ 7.3.

6~~7~~. The composition of claim 4~~5~~ or 5~~6~~ wherein the pH sensitive polymer is selected from the group consisting of hydroxypropylmethyl celluloses and anionic copolymers of methacrylic acid and methacrylmethacrylate.

7~~8~~. The composition according to any one of the preceding claims wherein the at least one compound is selected from the group consisting of compounds stimulating the enteroendocrine cells by a mechanism selected from the group consisting of transport into enteroendocrine cells by a transporter expressed by said cells wherein the transporter is selected from the group consisting of GLUT2 and SGLT1, and binding to G protein-coupled receptors expressed by said cells, the G protein-coupled receptors being preferably selected from bile acid receptors, amino acid receptors, peptide receptors and fatty acid receptors and taste receptors.

~~9. The composition of claim 8 wherein the G-protein-coupled receptor is selected from bile acid receptors, amino acid receptors, peptide receptors and fatty acid receptors and taste receptors~~.

8~~10~~. The composition of claim 7~~8 or 9~~ wherein said compound(s) is/are selected from the group consisting of carbohydrates, fatty acids, bile acids, peptides, amino acids, alcohol amides, and anthocyanins.

9~~11~~. The composition of claim 8~~10~~ wherein the core contains glucose, and optionally one or more compounds selected from sucralose, fatty acids having 2 to 6 carbon atoms, oleic acid, bile acids, peptides, amino acids, ethanolamides and anthocyanins.

10~~12~~. The composition of claim 9~~11~~ wherein the multiple dosage forms each have a glucose content of form 5 % (w/w) to 95 % (w/w). (w/w), preferably from 25 % (w/w) to 75 % (w/w), more preferably from 40 % (w/w) to 70 % (w/w).

11~~13~~. The composition of claim 9~~11~~ or 1012 containing 0.5 g to 30 g glucose, preferably 5 g to 20 g glucose, more preferably 7 g to 15 g glucose, per unit dose of the composition.

12~~14~~. The composition according to any one of the preceding claims wherein the enteroendocrine cells are selected from the group consisting of I cells, K cells and L cells.

13~~15~~. The composition according to any one of the preceding claims wherein the core further contains a substance, preferably caffeine, enhancing enterokine release by the enteroendocrine cells effected by the compound stimulating enteroendocrine cells

to release at least one enterokine, preferably the release of GLP-1 and/or PYY by L cells,

~~16. The composition of claim 15 wherein the substance enhances release of GLP-1 and/or PYY by L cells.~~

~~17. The composition of claim 16 wherein the substance is caffeine.~~

1418. The composition according to any one of the preceding claims wherein the core further contains an enteroendocrine cell maturation agent, preferably a human milk oligosaccharide (HMO).

~~19. The composition of claim 18 wherein the maturation agent is a human milk oligosaccharide (HMO).~~

1520. The composition according to any one of the preceding claims wherein the core contains at least one disintegrant providing a burst release of the ingredients of the core from the dosage form upon at least partial dissolving and/or degradation of the enteric coating.

1621. The composition according to any one of the preceding claims wherein the multiple dosage forms and the ~~one or more~~ gelling compositionagent are present in a liquid medium, preferably water or an aqueous solution.

~~22. The composition of claim 21 wherein the liquid medium is water or an aqueous solution.~~

1723. The composition according to any one of the preceding claims further comprising one or more pH modifiers, preferably contained in the gelling composition.

~~24 The composition according to any one of claims 1 to 20 wherein the one or more gelling agents is/are present in a gelling composition.~~

~~25. The composition of claim 24 wherein the gelling composition comprises one or more pH modifiers.~~

~~26. The composition of claims 24 or 25 the gelling composition and the multiple dosage forms form a heterogeneous mixture~~.

18~~27~~. A pharmaceutical article comprising multiple dosage forms as defined according to any one of claims 1 to 15~~20~~ and a gelling composition comprising at least one gelling agent and, optionally, one or more pH modifiers, wherein the multiple dosage forms and the ~~at least one~~ gelling compositionagent are physically separated.

~~28. The article of claim 27 wherein the at least one gelling agent is present in a gelling composition~~.

~~29. The article of claim 28 wherein the gelling composition further contains one or more pH modifiers.~~

19~~30~~. The article ~~according to any one~~ of claim~~s~~ 18~~27 to 29~~ further comprising a liquid medium physically separated from the multiple dosage forms and from the ~~at least one gelling agent or gelling~~ composition.

20~~31~~. The article ~~according to any one~~ of claim~~s~~ 18 or 19~~27 to 30~~ wherein the multiple dosage forms and the ~~at least one~~ gelling compositionagent and, optionally, the liquid medium, are provided in a single container comprising at least one compartment containing the multiple dosage form, at least one compartment containing the ~~at least one gelling agent or~~ gelling composition and, optionally, at least one compartment containing the water or aqueous solution, wherein said compartments are separated by a breakable physical separation.

21~~32~~. A pharmaceutical article comprising the composition according to any one of claims 1~~24~~ to 17~~26~~ and comprising a liquid medium physically separated from said composition.

22~~33~~. The article of claim 21~~32~~ wherein the composition and the liquid medium are provided in a single container comprising at least one compartment containing the composition and at least one compartment containing the liquid medium, wherein said compartments are separated by a breakable physical separation.

23~~34~~. The article according to any one of claims 18~~27~~ to 22~~33~~ wherein the liquid medium is water or an aqueous solution.

24.~~35~~ The composition according to any one of claims 1 to 17~~26~~ or the article according to any one of claim 18~~27~~ to 23~~31~~ ~~or the article according to any one of claims 32 to 34~~ for use in the prevention and/or treatment in a subject suffering from conditions and/or disorders and/or diseases associated with disturbed enterokine release by enteroendocrine cells and/or conditions and/or disorders and/or diseases amenable to increased enterokine release by enteroendocrine cells.

25~~36~~. The composition or article for use of claim 24~~35~~ wherein the condition, disorder or disease is selected from metabolic disorders, vascular disorders, neurodegenerative diseases, skeletal diseases and gastroenterologic disorders.

26~~37~~. The composition or article for use of claim 25~~36~~ wherein the metabolic disorder is selected from the group consisting of insulin resistance, type 2 diabetes mellitus, non-alcoholic fatty liver disease, non-alcoholic steatohepatosis, metabolic syndrome, hyperlipidemia and obesity; and/or~~.~~
wherein the vascular disorder is selected from microvascular dysfunction, cardiovascular diseases, cerebrovascular diseases and pulmonary vascular diseases; and/or
wherein the skeletal disease is osteoporosis, and/or
wherein the gastroenterological disorder is selected from the group consisting of impaired gastro-intestinal function and malabsorption conditions.

27~~38~~. The composition or article for use of claim 26~~37~~ wherein the metabolic disorder, is associated with adipose tissue inflammation.

~~39. The composition or article for use of claim 36 wherein the vascular disorder is selected from microvascular dysfunction, cardiovascular diseases, cerebrovascular diseases and pulmonary vascular diseases.~~

28~~40~~. The composition or article for use of claim 26~~39~~ wherein the pulmonary disease is associated with pneumonia.

29~~41~~. The composition or article for use of claim 28~~40~~ wherein the pneumonia is caused by or associated with a viral infection., preferably an infection by a coronavirus causing a respiratory condition, more preferably the viral infection is an infection by a

coronavirus selected from the group consisting of SARS-COV-1, SARS-COV-2 and MERS.

~~42. The composition or article for use of claim 41 wherein the viral infection is an infection by a coronavirus causing a respiratory condition.~~

~~43. The composition or article for use of claim 41 or 42 wherein the viral infection is an infection by a coronavirus selected from the group consisting of SARS-COV-1, SARS-COV-2 and MERS.~~

~~44. The composition or article for use of claim 36 wherein the skeletal disease is osteoporosis.~~

~~45. The composition or article for use of claim 36 wherein the gastroenterological disorder is selected from the group consisting of impaired gastro-intestinal function and malabsorption conditions.~~

3046. The composition or article for use according to any one of claims 2435 to 2945 wherein said condition, disorder or disease is accompanied by at least one condition selected from the group consisting of swallowing difficulty, impaired esophageal peristalsis, gastroparesis and impaired intestinal peristalsis.