FORMULATION FOR ORAL DELIVERY OF PROTEINS, PEPTIDES AND SMALL MOLECULES WITH POOR PERMEABILITY

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the priority of U.S. Provisional Application No. 62/832,508, filed April 11, 2019, the entire contents of which are incorporated herein by reference.

FIELD OF THE DISCLOSURE

[0002] This disclosure relates to a formulation for oral delivery of proteins, peptides and small molecules with poor permeability. More specifically, this disclosure relates to a pharmaceutical formulation intended for oral delivery of any molecule synthetic or natural with poor permeability or salts or solvates thereof having a therapeutic activity.

BACKGROUND OF THE INVENTION

[0003] Poorly permeable molecules are compounds that have poor absorption through the intestinal membrane. As such, they are administered intravenously or subcutaneously. Because of their poor absorption through the intestinal membrane, their clinical use is considerably restricted given the need to be administered IV and dosed several times a day (e.g., insulin for diabetics). These poorly permeable compounds are identified as BCS class III and class IV compounds in the classification proposed by Amidon GL et al in *A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability* (Pharm Res. 1995 Mar;12(3):413-20.), which is hereby incorporated by reference in its entirety.

SUMMARY

[0003a] In an aspect of the present disclosure, there is provided a pharmaceutical formulation, comprising:

a dispersed powder comprising a hydrophilic, synthetic or natural poorly permeable molecule or salt or solvate thereof in an amount 0.01-20 wt.% of the total weight of the formulation;

wherein the synthetic or natural poorly permeable molecule is a peptide or protein and is a BCS Class III or Class IV compound;

a lipophilic phase comprising triglycerides of fatty acids comprising medium chain fatty acids in an amount of 50-80 wt.% of the total weight of the formulation;

at least one hydrophilic surfactant with a hydrophilic lipophilic balance (“HLB”) above 10 in an amount of 1-30 wt.% of the total weight of the formulation; and

at least one lipophilic surfactant comprising partial esters of polyol and fatty acids comprising a mixture of mono and diglyceride of medium chain fatty acids in an amount of 10-50 wt.% of the total weight of the formulation,

wherein the pharmaceutical formulation does not include water.

[0003b] In another aspect of the present disclosure, there is provided a delayed release pharmaceutical dosage form comprising:

a pharmaceutical formulation comprising:

a dispersed powder comprising a hydrophilic, synthetic or natural poorly permeable molecule or salt or solvate thereof in an amount 0.01-20 wt. % of the total weight of the formulation, wherein the synthetic or natural poorly permeable molecule is a peptide or protein and is a BCS Class III or Class IV compound;

a lipophilic phase comprising triglycerides of fatty acids comprising medium chain fatty acids in an amount of 50-80 wt. % of the total weight of the formulation;

at least one hydrophilic surfactant with a hydrophilic lipophilic balance ("HLB") above 10 in an amount of 1-30 wt. % of the total weight of the formulation; and

at least one lipophilic surfactant comprising partial esters of polyol and fatty acids comprising a mixture of mono and diglyceride of medium chain fatty acids in an amount of 10-50 wt. % of the total weight of the formulation, wherein the delayed release dosage form is a coated dosage form whose release is pH dependent,

wherein the pharmaceutical formulation does not include water.

[0003c]In a further aspect of the present disclosure, there is provided a pharmaceutical formulation for use in therapy, wherein the pharmaceutical formulation comprises:

a dispersed powder comprising a hydrophilic, synthetic or natural poorly permeable molecule or salt or solvate thereof in an amount 0.01-20 wt. % of the total weight of the formulation, wherein the synthetic or natural poorly permeable molecule is a peptide or protein and is a BCS Class III or Class IV compound;

a lipophilic phase comprising triglycerides of fatty acids comprising medium chain fatty acids in an amount of 50-80 wt. % of the total weight of the formulation;

at least one hydrophilic surfactant with a hydrophilic lipophilic balance ("HLB") above 10 in an amount of 1-30 wt. % of the total weight of the formulation; and

at least one lipophilic surfactant comprising partial esters of polyol and fatty acids comprising a mixture of mono and diglyceride of medium chain fatty acids in an amount of 10-50 wt. % of the total weight of the formulation,

wherein the pharmaceutical formulation does not include water.

CLAIMS

1. A pharmaceutical formulation, comprising:

a dispersed powder comprising a hydrophilic, synthetic or natural poorly permeable molecule or salt or solvate thereof in an amount 0.01-20 wt.% of the total weight of the formulation;

wherein the synthetic or natural poorly permeable molecule is a peptide or protein and is a BCS Class III or Class IV compound;

a lipophilic phase comprising triglycerides of fatty acids comprising medium chain fatty acids in an amount of 50-80 wt.% of the total weight of the formulation;

at least one hydrophilic surfactant with a hydrophilic lipophilic balance ("HLB") above 10 in an amount of 1-30 wt.% of the total weight of the formulation; and

at least one lipophilic surfactant comprising partial esters of polyol and fatty acids comprising a mixture of mono and diglyceride of medium chain fatty acids in an amount of 10-50 wt.% of the total weight of the formulation,

wherein the pharmaceutical formulation does not include water.

2. The formulation of claim 1, wherein the peptide has from 5 to 20 amino acids.

3. The formulation of claim 1, wherein the at least one hydrophilic surfactant is selected from the group consisting of polyoxyethylene (20) monooleate, PEG 8 caprylic/capric glycerides, PEG 6 caprylic/capric glycerides, poly(oxyethylene)(4)Lauryl ether and mixtures thereof.

4. A delayed release pharmaceutical dosage form comprising:

a pharmaceutical formulation comprising:

a dispersed powder comprising a hydrophilic, synthetic or natural poorly permeable molecule or salt or solvate thereof in an amount 0.01-20 wt. % of the total weight of the formulation, wherein the synthetic or natural poorly permeable molecule is a peptide or protein and is a BCS Class III or Class IV compound;

a lipophilic phase comprising triglycerides of fatty acids comprising medium chain fatty acids in an amount of 50-80 wt. % of the total weight of the formulation;

at least one hydrophilic surfactant with a hydrophilic lipophilic balance ("HLB") above 10 in an amount of 1-30 wt. % of the total weight of the formulation; and

at least one lipophilic surfactant comprising partial esters of polyol and fatty acids comprising a mixture of mono and diglyceride of medium chain fatty acids in an amount of 10-50 wt. % of the total weight of the formulation, wherein the delayed release dosage form is a coated dosage form whose release is pH dependent,

wherein the pharmaceutical formulation does not include water.

5. A pharmaceutical formulation for use in therapy, wherein the pharmaceutical formulation comprises:

a dispersed powder comprising a hydrophilic, synthetic or natural poorly permeable molecule or salt or solvate thereof in an amount 0.01-20 wt. % of the total weight of the formulation, wherein the synthetic or natural poorly permeable molecule is a peptide or protein and is a BCS Class III or Class IV compound;

a lipophilic phase comprising triglycerides of fatty acids comprising medium chain fatty acids in an amount of 50-80 wt. % of the total weight of the formulation;

at least one hydrophilic surfactant with a hydrophilic lipophilic balance ("HLB") above 10 in an amount of 1-30 wt. % of the total weight of the formulation; and

at least one lipophilic surfactant comprising partial esters of polyol and fatty acids comprising a mixture of mono and diglyceride of medium chain fatty acids in an amount of 10-50 wt. % of the total weight of the formulation,

wherein the pharmaceutical formulation does not include water.

6. The pharmaceutical formulation for use of claim 8, wherein the peptide has from 5 to 20 amino acids.

7. The pharmaceutical formulation for use of claim 8, wherein the at least one hydrophilic surfactant is selected from the group consisting of polyoxyethylene (20) monooleate, PEG 8 caprylic/capric glycerides, PEG 6 caprylic/capric glycerides, poly(oxyethylene)(4)Lauryl ether and mixtures thereof.

8. The pharmaceutical formulation for use of claim 8, wherein the pharmaceutical formulation is in a delayed release dosage form comprising a coated dosage form whose release is pH dependent.