defined in BCS (i.e. the highest dose is soluble in 250 ml or less of water over a range of pH from 1 to 7.5). Examples of the hydrophilic drug include but are not limited to albuterol, ~~alendroate, amoxicillin,~~ bendamustine, ~~buspirone, calcitonin,~~ captopril, carboplatin, ciprofloxacin, ~~fluconazole, folic acid,~~ gemcitabine, ~~granisetron, hydrochlorothiazide,~~ ibandronate, lamivudine, ~~lamotrigine,~~ metformin, ~~metronidazole,~~ niacin, ~~oxaliplatin,~~ oxycodone, ~~parathyroid hormone (PTH), progesterone,~~ ranitidine, risedronate, rosiglitazone~~,~~ and sumatriptan~~,~~ ~~timolol maleate, and zoledronic acid~~. In some embodiments of the invention, the hydrophilic drug is bendamustine or gemcitabine. In a certain embodiment of the invention, the hydrophilic drug is present in an amount ranging from about 0.2% to about 15% (w/w) based on the weight of the pharmaceutical composition.

[0021] According to the invention, the one or more solvents as used herein are capable of dissolving a given hydrophilic drug or its pharmaceutically acceptable salt to form a drug-solvent solution. Particularly, each of the one or more solvents as used herein is capable of dissolving about 1 part of a given hydrophilic drug or its pharmaceutically acceptable salt in less than 100 parts of the solvent. More particularly, the one or more solvents as used herein may be selected from the group consisting of (a) a first solvent capable of dissolving about 1 part of a given hydrophilic drug or its pharmaceutically acceptable salt in less than about 1 part of the first solvent (very soluble); (b) a second solvent capable of dissolving about 1 part of a given hydrophilic drug or its pharmaceutically acceptable salt in about 1 to about 10 parts of the second solvent (free soluble); (c) a third solvent capable of dissolving about 1 part of a given hydrophilic drug or its pharmaceutically acceptable salt in about 10 to about 30 parts of the third solvent (soluble); (d) a forth solvent capable of dissolving about 1 part of a given hydrophilic drug or its pharmaceutically acceptable salt in about 30 to about 100 parts of the fourth solvent (sparingly soluble); and (e) any combination thereof. Generally, approximate quantity of solvent by volume is for one part of soluble by weight. For example, a first solvent is capable of dissolving about 1g of a given hydrophilic drug in less than 1 ml of the solvent. Examples of the solvent(s) as used herein include but are not limited to water, ethanol, polyethylene glycol (PEG), isopropanol (IPA), 1,2-propanediol (propylene glycol), glycerol, and acetic acid. Any of the solvents can be used alone or in combination. In one embodiment, the self micro-emulsifying pharmaceutical composition of the invention contains water as a solvent. In a certain embodiment of the invention, the one or more solvents are present in an amount ranging from about 2.5% to about 60% (w/w) based on the weight of the pharmaceutical composition.

CLAIMS

I/we claim:

1. An oral self micro-emulsifying pharmaceutical composition, which comprises:

(a) a therapeutically effective amount of a hydrophilic drug or its pharmaceutically acceptable salt;

(b) one or more solvents capable of dissolving the hydrophilic drug or its pharmaceutically acceptable salt to form a drug-solvent solution;

(c) a surfactant system comprising one or more surfactants, said surfactant system exhibiting a hydrophilic-lipophilic balance (HLB) value ranging from about 8 to about 17; and

(d) one or more hydrophilic carriers which are compatible with said drug-solvent solution and said surfactant system;

wherein the pharmaceutical composition is in a form of a self micro-emulsifying formulation for oral administration.

2. The oral self micro-emulsifying pharmaceutical composition of Claim 1, which forms an emulsion with a particle size of less than about 800 nm when said pharmaceutical composition contacts an aqueous medium.

3. The oral self micro-emulsifying pharmaceutical composition of Claim 1, wherein the hydrophilic drug is bendamustine or gemcitabine.

4. The oral self micro-emulsifying pharmaceutical composition of Claim 1, wherein each of the one or more solvents is capable of dissolving about 1 part of a given hydrophilic drug or its pharmaceutically acceptable salt in less than 100 parts of the solvent.

5. The oral self micro-emulsifying pharmaceutical composition of Claim 1, wherein the one or more solvents are selected from the group consisting of water, ethanol, polyethylene glycol (PEG), isopropanol (IPA), 1,2-propanediol (propylene glycol), glycerol, acetic acid, and any combinations thereof.

6. The oral self micro-emulsifying pharmaceutical composition of Claim 5, which comprises water as the solvent.

7. The oral self micro-emulsifying pharmaceutical composition of Claim 1, wherein the one or more surfactants are selected from the group consisting of polysorbate, poloxamers, oleoyl polyoxylglycerides, linoleoyl polyoxylglycerides, caprylocaproyl polyoxylglycerides, polyoxyethylene castor oil derivatives, polyoxyethylene alkyl ethers, sorbitan fatty acid esters, glyceryl monooleate, glyceryl monolinoleate, medium-chain triglycerides (MCT), polyglyceryl oleate, lauroyl polyoxylglyceride, stearoyl polyoxylglycerides, propylene glycol dicaprylocaprate,

propylene glycol laurate, propylene glycol monolaurate, propylene glycol caprylate and propylene glycol monocaprylate, and combinations thereof.

8. The oral self micro-emulsifying pharmaceutical composition of Claim 7, which comprise polysorbate and oleoyl polyoxylglycerides as the surfactants.

9. The oral self micro-emulsifying pharmaceutical composition of Claim 1, wherein each of the one or more hydrophilic carriers is capable of dissolving about 1 part of a given hydrophilic drug or its pharmaceutically acceptable salt in about 10 to about 10,000 parts of the hydrophilic carrier.

10. The oral self micro-emulsifying pharmaceutical composition of Claim 1, wherein the one or more hydrophilic carriers are selected from the group consisting of polysorbate, ethanol, polyethylene glycol (PEG), glycerol, 1,2-propanediol (propylene glycol), propylene carbonate (PC), diethylene glycol monoethyl ether, and combinations thereof.

11. The oral self micro-emulsifying pharmaceutical composition of Claim 10, which comprises glycerol and PEG as the hydrophilic carriers.

12. The oral self micro-emulsifying pharmaceutical composition of Claim 10, which comprises propylene glycol and PEG as the hydrophilic carriers.

13. The oral self micro-emulsifying pharmaceutical composition of Claim 3, which has a pH above the 4.0.

14. The oral self micro-emulsifying pharmaceutical composition of Claim 1, which comprises gemcitabine or its pharmaceutically acceptable salt, water, glycerol, PEG, polysorbate, and oleoyl polyoxylglycerides.

15. The oral self micro-emulsifying pharmaceutical composition of Claim 1, which comprises gemcitabine or its pharmaceutically acceptable salt, water, propylene glycol, PEG, polysorbate, and oleoyl polyoxylglycerides.

16. The oral self micro-emulsifying pharmaceutical composition of Claim 1, which comprises gemcitabine or its pharmaceutically acceptable salt, water, glycerol, PEG, polysorbate, oleoyl polyoxylglycerides, and TPGS.

17. A method for preparing an oral self micro-emulsifying pharmaceutical composition of claim 1, comprising mixing together the hydrophilic drug or its pharmaceutically acceptable salt thereof, the one or more solvents, the one or more hydrophilic carriers and the surfactant system to form the oral self micro-emulsifying pharmaceutical composition..

18. The method of clam 17, comprising mixing the hydrophilic drug or its pharmaceutically acceptable salt thereof with the one or more solvents and the one or more hydrophilic carriers first and further with the surfactant system.

Claims

1. An oral self micro-emulsifying pharmaceutical composition, which comprises:

(a) a therapeutically effective amount of a hydrophilic drug or its pharmaceutically acceptable salt, which is selected from the group consisting of albuterol, bendamustine, captopril, carboplatin, ciprofloxacin, gemcitabine, ibandronate, lamivudine, metformin, niacin, oxycodone, ranitidine, and sumatriptan;

(b) one or more hydrophilic solvents capable of dissolving the hydrophilic drug or its pharmaceutically acceptable salt to form a drug-solvent solution;

(c) a surfactant system comprising one or more surfactants, said surfactant system exhibiting a hydrophilic-lipophilic balance (HLB) value ranging from about 8 to about 17; and

(d) one or more hydrophilic carriers which are compatible with said drug-solvent solution and said surfactant system;

wherein the pharmaceutical composition forms a substantially homogenous solution that is free of a drug-containing oily phase as a self micro-emulsifying formulation for oral administration.

2. The oral self micro-emulsifying pharmaceutical composition of Claim 1, which forms an emulsion with a particle size of less than about 800 nm when said pharmaceutical composition contacts an aqueous medium.

3. The oral self micro-emulsifying pharmaceutical composition of Claim 1 or 2, wherein the hydrophilic drug is bendamustine or gemcitabine.

4. The oral self micro-emulsifying pharmaceutical composition of any one of Claims 1-3, wherein each of the one or more solvents is capable of dissolving about 1 part of a given hydrophilic drug or its pharmaceutically acceptable salt in less than 100 parts of the solvent.

5. The oral self micro-emulsifying pharmaceutical composition of any one of Claims 1-4, wherein the one or more solvents are selected from the group consisting of water, ethanol, polyethylene glycol (PEG), isopropanol (IPA), 1,2-propanediol (propylene glycol), glycerol, acetic acid, and any combinations thereof.

6. The oral self micro-emulsifying pharmaceutical composition of Claim 5, which comprises water as the solvent.

7. The oral self micro-emulsifying pharmaceutical composition of any one of Claims 1-6, wherein the one or more surfactants are selected from the group consisting of polysorbate, poloxamers, oleoyl polyoxylglycerides, linoleoyl polyoxylglycerides, caprylocaproyl polyoxylglycerides, polyoxyethylene castor oil derivatives, polyoxyethylene alkyl ethers, sorbitan fatty acid esters, glyceryl monooleate, glyceryl monolinoleate, medium-chain triglycerides (MCT), polyglyceryl oleate, lauroyl polyoxylglyceride, stearoyl polyoxylglycerides, propylene glycol

dicaprylocaprate, propylene glycol laurate, propylene glycol monolaurate, propylene glycol caprylate and propylene glycol monocaprylate, and combinations thereof.

8. The oral self micro-emulsifying pharmaceutical composition of Claim 7, which comprise polysorbate and oleoyl polyoxylglycerides as the surfactants.

9. The oral self micro-emulsifying pharmaceutical composition of any one Claims 1-8, wherein each of the one or more hydrophilic carriers is capable of dissolving about 1 part of a given hydrophilic drug or its pharmaceutically acceptable salt in about 10 to about 10,000 parts of the hydrophilic carrier.

10. The oral self micro-emulsifying pharmaceutical composition of any one of Claims 1-9, wherein the one or more hydrophilic carriers are selected from the group consisting of polysorbate, ethanol, polyethylene glycol (PEG), glycerol, 1,2-propanediol (propylene glycol), propylene carbonate (PC), diethylene glycol monoethyl ether, and combinations thereof.

11. The oral self micro-emulsifying pharmaceutical composition of Claim 10, which comprises glycerol and PEG as the hydrophilic carriers.

12. The oral self micro-emulsifying pharmaceutical composition of Claim 10, which comprises propylene glycol and PEG as the hydrophilic carriers.

13. The oral self micro-emulsifying pharmaceutical composition of Claim 3, which has a pH above the 4.0.

14. The oral self micro-emulsifying pharmaceutical composition of Claim 1, which comprises gemcitabine or its pharmaceutically acceptable salt, water, glycerol, PEG, polysorbate, and oleoyl polyoxylglycerides.

15. The oral self micro-emulsifying pharmaceutical composition of Claim 1, which comprises gemcitabine or its pharmaceutically acceptable salt, water, propylene glycol, PEG, polysorbate, and oleoyl polyoxylglycerides.

16. The oral self micro-emulsifying pharmaceutical composition of Claim 1, which comprises gemcitabine or its pharmaceutically acceptable salt, water, glycerol, PEG, polysorbate, oleoyl polyoxylglycerides, and D-α-tocopheryl polyethylene glycol 1000 succinate (TPGS).

17. The oral self micro-emulsifying pharmaceutical composition of Claim 1, which comprises

(i) from 0.20% to 15% (w/w) of the hydrophilic drug or a pharmaceutically acceptable salt thereof;

(ii) from 2.5% to 60% (w/w) of the solvent;

(iii) from 20% to 75% (w/w) of the surfactant system; and

(iv) from 2.0% to 60% (w/w) of the carrier,

wherein the % (w/w) values are based on the total weight of the pharmaceutical composition.

18. The oral self micro-emulsifying pharmaceutical composition of any of Claims 1-17, wherein the ratio (solvent: carrier: surfactant system) is 2: 3: 4.5 by weight.

19. The oral self micro-emulsifying pharmaceutical composition of any of Claims 1-18, which forms an emulsion with a particle size of less than 200 nm when said pharmaceutical composition contacts an aqueous medium.

20. The oral self micro-emulsifying pharmaceutical composition of Claim 14, wherein the gemcitabine is present in an amount of 2.00% (w/w); water is present in an amount of 20.00% (w/w); glycerol and PEG are together present in an amount of 32.30% (w/w); and polysorbate and oleoyl polyoxylglycerides are together present in an amount of 45.70% (w/w), wherein the % (w/w) values are based on the total weight of the pharmaceutical composition.

21. The oral self micro-emulsifying pharmaceutical composition of Claim 15, wherein gemcitabine is present in an amount of 2.00% (w/w); water is present in an amount of 20.00% (w/w); propylene glycol and PEG are together present in an amount of 32.30% (w/w); and polysorbate and oleoyl polyoxylglycerides are together present in an amount of 45.70% (w/w), wherein the % (w/w) values are based on the total weight of the pharmaceutical composition.

22. The oral self micro-emulsifying pharmaceutical composition of Claim 16, wherein gemcitabine is present in an amount of 1.98% (w/w); water is present in an amount of 19.8% (w/w); glycerol and PEG are together present in an amount of 31.98% (w/w); polysorbate and oleoyl polyoxylglycerides are together present in an amount of 45.25% (w/w); and TPGS is present in an amount of 0.99% (w/w), wherein the % (w/w) values are based on the total weight of the pharmaceutical composition.

23. A method for preparing an oral self micro-emulsifying pharmaceutical composition of any of claims 1-22, comprising mixing together the hydrophilic drug or its pharmaceutically acceptable salt thereof, the one or more solvents, the one or more hydrophilic carriers and the surfactant system to form the oral self micro-emulsifying pharmaceutical composition.

24. The method of clam 23, comprising mixing the hydrophilic drug or its pharmaceutically acceptable salt thereof with the one or more solvents and the one or more hydrophilic carriers first and further with the surfactant system.

25. The method of claim 23, wherein no heating step is conducted to form the liquid oral self micro-emulsifying pharmaceutical composition.