Additionally, the disclosure provides a process for the formation of a pre-formulation as defined herein, suitable for the administration of a bioactive agent to a (preferably mammalian) subject, said process comprising forming a non-liquid crystalline, low viscosity mixture of

i) at least one ester of a sugar or sugar derivative;

ii) at least one phospholipid;

iii) at least one biocompatible, oxygen containing, low viscosity organic solvent;

and dissolving or dispersing at least one bioactive agent in the low viscosity mixture, or in at least one of components i), ii) or iii) prior to forming the low viscosity mixture wherein the pre-formulation does not further comprise a liquid crystal hardener.

The disclosure also provides the use of a non-liquid crystalline, low viscosity mixture of:

i) at least one ester of a sugar or sugar derivative;

ii) at least one phospholipid;

iii) at least one biocompatible, oxygen containing, low viscosity organic solvent;

wherein at least one bioactive agent is dissolved or dispersed in the low viscosity mixture in the manufacture of a pre-formulation for use in the sustained delivery of said active agent, wherein said pre-formulation is capable of forming at least one non-lamellar liquid crystalline phase structure upon contact with an aqueous fluid and wherein the pre-formulation does not further comprise a liquid crystal hardener.

The disclosure further provides a method of treatment or prophylaxis of a human or non-human (preferably mammalian) animal subject comprising administration of a pre-formulation as defined herein.

In another aspect, there is provided a pre-filled administration device containing a pre-formulation as defined herein.

CLAIMS:

1. A pre-formulation comprising a low viscosity, non-liquid crystalline, mixture of:
i) at least one sorbitan ester;
ii) at least one phospholipid;
iii) at least one biocompatible, oxygen containing, low viscosity organic solvent;
wherein component iii) comprises or consists of ethanol, DMSO, NMP or mixtures thereof;
wherein the pre-formulation forms, or is capable of forming, at least one non-lamellar liquid crystalline phase structure upon contact with an aqueous fluid;
and wherein the pre-formulation does not further comprise triglyerides, retinyl palmitate, benzyl benzoate, cholesterol, ubiquinone, tocopherols or mixtures thereof.

2. A pre-formulation according to claim 1 which does not comprise any component free of an ionizable group, having a hydrophobic moiety of 15 to 40 carbon atoms with a triacyl group or a carbon ring structure.

3. A pre-formulation according to claim 1 or claim 2 wherein component i) comprises at least one fatty acid ester of a sorbitan comprising a sorbitan head group and one to three fatty acyl tail groups.

4. A pre-formulation as claimed in claim 3 wherein component i) comprises at least one fatty acid sorbitan di-ester comprising a sorbitan head group and two fatty acyl tail groups.

5. A pre-formulation according to claim 3 or claim 4 wherein each fatty acyl tail group is independently selected from caproic, caprylic, capric, lauric, myristic, palmitic, phytanic, palmitolic, stearic, iso-stearic, oleic, elaidic, linoleic, linolenic, arachidonic, behenic or lignoceric acids.

6. A pre-formulation according to claim 3 or claim 4 wherein each fatty acyl tail group is oleic acid.

7. A pre-formulation according to any one of the preceding claims wherein component ii) is at least one phosphatidyl choline or at least one phosphatidyl ethanolamine or mixtures thereof.

8. A pre-formulation according to any one of the preceding claims wherein the weight ratio of i) : ii) is in the range of 30:70 to 80:20.

9. A pre-formulation according to claim 8 wherein component i) comprises at least 30% fatty acid di-esters of sorbitan and component ii) is soy phosphatidylcholine, wherein the weight ratio of i) : ii) is 45:55 to 75:25.

10. A pre-formulation according to any one of the preceding claims having a viscosity of below 1000 mPas at 20°C.

11. A pre-formulation according to any one of the preceding claims further comprising at least one active agent.

12. A pre-formulation according to claim 11 wherein said active agent is a peptide active agent.

13. A pre-formulation as claimed in claim 11 or claim 12 wherein said active agent is selected from opioid agonists, opioid antagonists, GnRH agonists, GnRH antagonists, somatostatins and somatostatin receptor (SSTR) agonists, glucagon-like peptide 1 (GLP-1) receptor agonists, and glucagon-like peptide 2 agonists, and mixtures thereof.

14. A pre-formulation according to claim 11 wherein the active agent is an opioid agonist selected from buprenorphine, fentanyl, sufentanil, remifentanil, oxymorphone, dimorphone, dihydroetorphine or diacetylmorphine; or wherein the active agent is an opioid antagonist selected from naloxone, nalmefene or naltrexone.

15. A pre-formulation according to claim 11 wherein said active agent is a cyclic peptide of 30 or fewer amino acids.

16. A pre-filled administration device containing a pre-formulation as claimed in any one of claims 1 to 15.

17. A kit comprising an administration device as claimed in claim 16.