SUMMARY

[0003a] In one aspect, there is provided a lipid-based particle composition, comprising: a nanoparticle comprising: a therapeutic agent; a phospholipid at a weight percent in the composition ranging from 2.5% to 20%; a sterol at a weight percent in the composition ranging from 0.25% to 10%; and a lipid component other than a phospholipid at a weight percent in the composition ranging from 2.5% to 20%; and water; wherein the nanoparticles have an average size ranging from about 75 nm to about 500 nm; and wherein, upon storage for a period of one month, the average size of the nanoparticles changes by less than about 20%.

[003b] In another aspect, there is provided a lipid-based particle composition, comprising: a particle comprising: a therapeutic agent; a phospholipid at a weight percent in the composition ranging from 5% to 60%; a sterol at a weight percent in the composition ranging from 1% to 25%; and a lipid component other than a phospholipid at a weight percent in the composition ranging from 5% to 50%; wherein the nanoparticles have an average size ranging from about 75 nm to about 500 nm; and wherein, upon storage for a period of one month, the average size of the nanoparticles changes by less than about 20%.

[0004] Some examples disclosed herein pertain to a particle composition and/or a lipid-based particle composition for the delivery of an active agent. In some examples, the particle is a lipid particle. In some examples, the particle is a nanoscale particle. In some examples, the particle is a microscale particle. In some examples, the particle is liposomal (e.g., is a liposome). In some examples, the particle comprises one or more of a phospholipid component, a non-phospholipid lipid component (e.g., a medium and/or long chain triglyceride component), a sterol component, and/or water. In some examples, the particle further comprises the active ingredient (e.g., a therapeutic agent). In some examples, the active ingredient is a phytocannabinoid. In some examples, the phytocannabinoid is CBD. In some examples, the lipid constituents of the particle allow it to solubilize CBD of high purity. In some examples, the CBD in the particle is of sufficient purity to provide a crystalline and/or solid (e.g., an amorphous or crystalline powder). In some examples, the CBD not an oil.

[0005] In some examples, the phytocannabinoid of a lipid-based particle composition as disclosed herein is a single phytocannabinoid (e.g., CBD). In some examples, the phytocannabinoid (e.g., CBD) has a purity by weight % of equal to or greater than about: 95%, 97%, 98%, 99%, 100%, or ranges including and/or spanning the aforementioned values. In some examples, the phytocannabinoid (e.g., CBD) is present in the lipid-based particle composition at dry weight % of equal to or greater than about: 5%, 8%, 10%, 15%, 20%, or ranges including and/or spanning the aforementioned values. In some examples, the phytocannabinoid is free of or essentially free of THC. In some examples, the phytocannabinoid (e.g., CBD) has a THC content by weight % of equal to or less than about: 1%, 0.5%, 0.25%, 0.1%, 0%, or ranges including and/or spanning the aforementioned values. In some examples, where present, THC is present below the limit of quantitation (LOQ) (e.g., when analyzed by high pressure liquid chromatography (HPLC) with standard detectors, such as UV/Vis, photodiode array, refractive index, fluorescence, light scattering, conductivity, and the like).

[0006] In some examples, the phospholipid component comprises one or more of phosphatidic acid, phosphatidylethanolamine, phosphatidylcholine, phosphatidylserine, phosphatidylinositol, phosphatidylinositol phosphate, phosphatidylinositol bisphosphate, and phosphatidylinositol trisphosphate. In some examples, the phospholipid component comprises phosphatidylcholine. In some examples, the phospholipid component is a single phospholipid. In some examples, the phospholipid component is phosphatidylcholine. In some examples, the phosphatidylcholine is highly pure. In some examples, the phosphatidylcholine has a purity by weight % of equal to or greater than about: 97%, 98%, 99%, 100%, or ranges including and/or spanning the aforementioned values. In some examples, the phosphatidylcholine is present in the lipid-based particle composition at dry weight % of equal to or greater than about: 10%, 20%, 30,%, 35%, 40%, 45%, 50%, or ranges including and/or spanning the aforementioned values.

[0007] In some examples, the lipid component comprises a triglyceride. In some examples, the lipid component comprises a medium chain triglyceride (MCT). In some examples, the medium chain triglyceride comprises a fatty acid selected from one or more of caprioc acid, octanoic acid, capric acid, caprylic acid, and/or lauric acid (e.g., is formed from). In some examples, the medium chain triglyceride comprises a fatty acid 6-12 carbons in length (e.g., 6, 7, 8, 9, 10, 11, or 12). In some examples, the lipid component comprises a long chain triglyceride. In some examples, the long chain triglyceride comprises a fatty acid greater than 12 carbons in length (e.g., greater than or equal to 13, 14, 15, 16, 17, 18, 19, or 20 carbons in length, or ranges including and/or spanning the aforementioned values). In some examples, the lipid component is a single lipid. In some examples, the lipid component is MCT. In some examples, the MCT is highly pure. In some examples, the MCT has a purity by weight % of equal to or greater than about: 90%, 95%, 97%, 98%, 99%, 100%, or ranges including and/or spanning the aforementioned values. In some examples, the MCT (or LCT) is present in the lipid-based particle composition at dry weight % of equal to or greater than about: 10%, 20%, 30%, 35%, 40%, 45%, 50%, or ranges including and/or spanning the aforementioned values.

[0008] In some examples, the sterol component comprises cholesterol. In some examples, the sterol component is a single sterol. In some examples, the sterol

component is cholesterol. In some examples, the cholesterol (or other sterol) is highly pure. In some examples, the cholesterol (or other sterol) has a purity by weight % of equal to or greater than about: 97%, 98%, 99%, 100%, or ranges including and/or spanning the aforementioned values. In some examples, the cholesterol (or other sterol) is present in the lipid-based particle composition at dry weight % of equal to or greater than about: 1%, 2%, 4%, 5%, 8%, or ranges including and/or spanning the aforementioned values.

[0009] In some examples, the lipid-based particle composition is aqueous while in other examples the composition may be provided as a dry or substantially dry solid (e.g., having a water content in weight % of less than or equal to 20%, 15%, 10%, 5%, 2%, 1%, 0.5%, or ranges including and/or spanning the aforementioned values). In some examples, where the lipid-based particle composition is aqueous, water may be present at a wet weight percent of equal to or less than about: 70%, 75%, 77%, 80%, 85%, or ranges including and/or spanning the aforementioned values. In some examples of the aqueous composition, the phytocannabinoid (e.g., CBD) is present in the composition at wet weight % of equal to or greater than about: 1%, 2%, 5%, 8%, 10%, 15%, 20%, or ranges including and/or spanning the aforementioned values. In some examples, the phosphatidylcholine is present in the aqueous composition at wet weight % of equal to or greater than about: 5%, 10%, 15%, 20%, or ranges including and/or spanning the aforementioned values. In some examples, the MCT is present in the aqueous composition at wet weight % of equal to or greater than about: 5%, 10%, 15%, 20%, or ranges including and/or spanning the aforementioned values. In some examples, the cholesterol is present in the aqueous composition at wet weight % of equal to or greater than about: 0.5%, 1.0%, 2.0%, 3.0%, 5.0%, or ranges including and/or spanning the aforementioned values.

[0010] In some examples, as disclosed elsewhere herein, the particle comprises CBD, phosphatidylcholine, cholesterol, a lipid component other than a phospholipid (e.g., one or more of a medium chain triglyceride, a long chain triglyceride, and/or hemp oil), and/or water. In some examples, the CBD is present in an amount of less than or equal to about 25 mg/ml. In some examples, the phosphatidylcholine is present in an amount of less than or equal to about 100 mg/ml. In some examples, the cholesterol is present in an amount of less than or equal to about 25 mg/ml. In some

examples, the medium chain triglyceride is present in an amount of less than or equal to about 100 mg/ml.

[0011] In some examples, the lipid-based particle composition further comprises a preservative. In some examples, the preservative comprises one or more of malic acid, citric acid, potassium sorbate, sodium benzoate, and Vitamin E. In some examples, malic acid is present in an amount of less than or equal to about 0.85 mg/ml. In some examples, citric acid is present in an amount of less than or equal to about 0.85 mg/ml. In some examples, potassium sorbate is present in an amount of less than or equal to about 1 mg/ml. In some examples, sodium benzoate is present in an amount of less than or equal to about 1 mg/ml. In some examples, the composition further comprises a flavoring agent.

[0012] Some examples pertain to a lipid-based particle composition, comprising: a nanoparticle comprising: cannabidiol (CBD) that is of sufficient purity that it exists in a solid and/or powdered state prior to formulation in the nanoparticle composition at a weight percent in the composition ranging from 1% to 10%; a phosphatidylcholine at a weight percent in the composition ranging from 2.5% to 15%; a sterol at a weight percent in the composition ranging from 0.5% to 5%; and a medium chain triglyceride at a weight percent in the composition ranging from 2.5% to 15%. In some examples, the composition comprises water at a weight percent in the composition ranging from 60% to about 80%. In some examples, the nanoparticles have an average size ranging from about 75 nm to about 175 nm. In some examples, upon storage for a period of one month, the average size of the nanoparticles changes by less than about 20%.

[0013] In some examples, the lipid-based particle composition is in the form of liposomes and/or an oil-in-water nano-emulsion. In some examples, an appreciable amount of the nanoparticle composition does not settle and/or separate from the water upon standing for a period of at least about 12 hours. In some examples, the composition is configured such that when concentrated to dryness to afford a powder formulation of nanoparticles, the nanoparticle powder can be reconstituted to provide the nanoparticle composition. In some examples, the composition has a Tmax for CBD of less than 4.5 hours. In some examples, upon storage for a period of one month, the average size of the nanoparticles changes by less than about 20%. In some examples, the polydispersity of

the nanoparticles in the composition is less than or equal to 0.15. In some examples, upon 90 days of storage at 25°C and 60% relative humidity, the polydispersity of the nanoparticles changes by less than or equal to 10%. In some examples, upon 90 days of storage at 25°C and 60% relative humidity, the polydispersity of the nanoparticles changes by less than or equal to 0.1. In some examples, the composition has a shelf life of greater than 18 months at 25°C and 60% relative humidity. In some examples, upon 90 days of storage at 25°C and 60% relative humidity, the D90 of the nanoparticles changes less than or equal to 10%. In some examples, the composition has a concentration max (Cmax) of 80 ng/ml after an oral dose of 15 mg/kg.

[0014] Some examples, pertain to a lipid-based particle composition, comprising a particle comprising cannabidiol (CBD) that is of sufficient purity that it exists in a solid and/or powdered state prior to formulation in the nanoparticle composition at a weight percent in the composition ranging from 5% to 15%, a phosphatidylcholine at a weight percent in the composition ranging from 35% to 60%, a sterol at a weight percent in the composition ranging from 2.5% to 10%, and a medium chain triglyceride at a weight percent in the composition ranging from 35% to 50%. In some examples, the composition further comprising a preservative. In some examples, the preservative comprises one or more of malic acid, citric acid, potassium sorbate, sodium benzoate, and Vitamin E. In some examples, the sterol is cholesterol. In some examples, the composition further comprises a flavoring agent.

[0015] In some examples, the composition has a Cmax of 80 ng/ml after an oral dose of 15 mg/kg. In some examples, the lipid-based particle composition is provided as a dry powder. In some examples, the powder is configured to be reconstituted in water to provide an aqueous solution. In some examples, wherein, upon reconstitution, nanoparticles within the aqueous solution have an average size ranging from about 75 nm to about 175 nm.

[0016] In some examples, the composition further comprising a preservative. In some examples, the preservative comprises one or more of malic acid, citric acid, potassium sorbate, sodium benzoate, and Vitamin E. In some examples, the sterol is cholesterol. In some examples, the composition further comprises a flavoring agent.

[0017] In some examples, as disclosed elsewhere herein, the lipid-based particle composition is in the form and/or comprises one or more of liposomes, an oil-in-water nano-emulsion (and/or microparticle emulsion), and/or solid lipid particles. In some examples, when suspended in water, an appreciable amount of the particles in the composition do not settle and/or do not separate (e.g., upon visual inspection) from the water upon standing for a period of at least about 12 hours. In some examples, when suspended in water, the particles remain substantially homogenously distributed in the water upon standing for a period of at least about 12 hours. In some examples, the nanoparticles have an average size ranging from about 10 nm to about 500 nm. In some examples, the composition comprises nanoparticles having an average size of less than or equal to about: 10 nm, 50 nm, 100 nm, 250 nm, 500 nm, 1000 nm, or ranges including and/or spanning the aforementioned values. In some examples, the composition comprises microparticles having an average size of less than or equal to about: 1000 nm, 1.5 µm, 2 µm, 3 µm, 5 µm, 10 µm or ranges including and/or spanning the aforementioned values. In some examples, the dried powder composition comprises microparticles that form nanoparticles (as disclosed herein) when reconstituted. In some examples, these dried powder compositions comprise particles having an average size of less than or equal to about: 250 nm, 500 nm, 1000 nm, 1.5 µm, 2 µm, 3 µm, 5 µm, 10 µm, 50 µm, or ranges including and/or spanning the aforementioned values. In some examples, upon storage for a period of one month, the average size of the nanoparticles (or microparticles) increases by less than about 10%.

[0018] In some examples, the lipid-based particle composition is configured such that when concentrated to dryness to afford dry particles (e.g., from any one of the oil-in-water emulsion (e.g., a nanoemulsion or microemulsion), liposome solution, and/or solid lipid particle) as a powder, the dry nanoparticles can be reconstituted to provide a reconstituted particle based solution (e.g., the nanoparticle composition). In some examples, when reconstituted, the average size of the nanoparticles increases or decreases by less than about 15% and/or by less than about 100%. In some examples, to form powders, excipients (and/or additives as disclosed elsewhere herein) may be added to the liposomes, oil-in-water nano-emulsions (and/or microparticle emulsions), and/or a solid lipid particle. In some examples, the excipient comprises trehalose.

[0019] Some examples, as disclosed elsewhere herein, pertain to a method of manufacturing a lipid-based particle composition. In some examples, one or more phytocannabinoids (e.g., CBD) is mixed with one or more lipophilic components of the composition to provide a solution. In some examples, one or more lipid components (that are not phospholipids) are added. In some examples, one or more sterols are added. In some examples, one or more phospholipids are added. In some examples, one or more flavoring and/or preservatives are added. In some examples, water is added. In some examples, the lipophilic ingredients are combined and the hydrophilic ingredients are combined separately. In some examples the lipophilic ingredients are then added to the hydrophilic ingredients. In some examples, the solution is passed through a microfluidizer and/or a high sheer homogenizer. In some examples, the process affords a particle composition.

[0020] In some examples, a method of manufacturing the particle composition of a phytocannabinoid is disclosed. In some examples, the phytocannabinoid is added to solvent. In some examples, one or more phospholipids are added to the solvent. In some examples, one or more sterols are added to the solvent. In some examples, one or more lipids is added to the solvent. In some examples, the solvent is removed to provide a substantially solid product. In some examples, the product is mixed with water to provide an emulsion. In some examples, the emulsion is passed through a microfluidizer and/or a high sheer homogenizer. In some examples, the process affords a nanoparticle composition.

[0021] Some examples pertain to a method of treating a patient in need of treatment comprising administering an effective amount therapeutic agent provided as a lipid-based particle composition as disclosed herein to the patient. Some examples pertain to a method of treating a patient in need of treatment comprising administering an effective amount of the composition to the patient. In some examples, the patient in need of treatment is a patient suffering from one or more of pain, anxiety & stress, seizures, malaise, inflammation, mood disorders, and insomnia. In some examples, the condition is treated by administering an effective amount of a composition as disclosed herein to the patient.

[0021a] In another aspect, there is provided use of the lipid-based particle composition as defined herein in the manufacture of a medicament for treating a condition in a patient.

[0022] In some examples, the Cmax is increased relative to CBD alone or comparator examples (e.g., CBD oil-based products) by equal to or at least about: 15%, 20%, 50%, 100%, 150%, 200%, or ranges including and/or spanning the aforementioned values. In some examples, the Cmax is increased (relative to an oil-based product) by equal to or at least about: 10 ng/mL, 20 ng/mL, 30 ng/mL, 40 ng/mL, 50 ng/mL, 60 ng/mL, 70 ng/mL, 80 ng/mL, 90 ng/mL, or ranges including and/or spanning the aforementioned values.

[0023] In some examples, the Tmax for CBD is decreased (relative to CBD alone or a CBD in oil mixture) by equal to or at least about: 15%, 20%, 50%, 100%, 150%, 200%, or ranges including and/or spanning the aforementioned values. In some examples, the Tmax for CBD in a disclosed example is decreased (relative to CBD alone or a CBD in oil mixture) by equal to or at least about: 15 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, or ranges including and/or spanning the aforementioned values.

[0024] In some examples, the AUC for CBD using a disclosed example is increased (relative to CBD alone or a CBD in oil mixture) by equal to or at least about: 100 ng/mL*hr, 200 ng/mL*hr, 300 ng/mL*hr, 400 ng/mL*hr, or ranges including and/or spanning the aforementioned values. In some examples, the AUC is improved (relative to CBD alone or a CBD in oil mixture) by equal to or at least about: 25%, 50%, 100%, 150%, 200%, or ranges including and/or spanning the aforementioned values.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] Figure 1 is a flow chart showing an embodiment of a method of preparing a lipid-based particle composition as disclosed herein.

[0026] Figure 2 is a flow chart showing another embodiment of a method for preparing a lipid-based particle composition as disclosed herein.

[0027] Figure 3 depicts the CBD concentration in an embodiment of the disclosed lipid-based particle compositions over time when stored at 25°C/60% relative humidity.

[0028] Figure 4 depicts the particle size of an embodiment of the disclosed lipid-based particle compositions over time when stored at 25°C/60% relative humidity.

[0029] Figures 5A-5E depict representative images of some embodiments of lipid nanoparticles as disclosed herein.