CLAIMS

What is claimed is:

1. A microsphere formulation, comprising:

   polymer microspheres, each polymer microsphere comprising:

   (i) esketamine or ketamine; and

   (ii) a biodegradable poly(lactide) polymer having an inherent viscosity of 0.6 dL/g ± 10% to 0.7 dL/g ± 10%,

   wherein each polymer microsphere has a drug load of esketamine or ketamine of 12 wt/wt% ± 10% to 17 wt/wt% ± 10%;

   wherein the polymer microspheres have a particle size of greater than 60 μm (D_{50}); and

   wherein the polymer microspheres are characterized in that:

   (i) each of the polymer microspheres comprises a plurality of internal macrovoids; and

   (ii) 80% to 100% of the esketamine or ketamine is released within 20 to 30 days of injection into a subject, but not more than 10% of the esketamine or ketamine is released within 24 hours of injection into the subject.

2. The microsphere formulation of claim 1, wherein the polymer microspheres are characterized in that the esketamine or ketamine exhibits an in vivo average release rate from the polymer microspheres of from 2.5% ± 10% to 3.5% ± 10% per day over a 30 day period in a human.

3. A method for making the polymer microspheres of claim 1 or 2, the method comprising:

(i) contacting esketamine or ketamine with the biodegradable poly(lactide) polymer in the presence of a solvent to form an organic component and providing the organic component to a first homogenizer;

(ii) providing an inner aqueous component comprising water and a first surfactant to the first homogenizer;

(iii) homogenizing the organic component with the inner aqueous component to form a primary emulsion;

(iv) providing the primary emulsion to a second homogenizer at a first flow rate;

(v) providing a continuous phase comprising water and a second surfactant to the second homogenizer at a second flow rate;

(vi) homogenizing the primary emulsion and the continuous phase; and

(vii) removing the solvent to form the polymer microspheres,

wherein each of the formed polymer microspheres incorporates at least a portion of the inner aqueous component in the form of a plurality of emulsions.

4. The method of claim 3, further comprising dehydrating the polymer microspheres, wherein the dehydrated polymer microspheres are characterized in that each of the polymer microspheres comprises a plurality of internal macrovoids.
5. The method of claim 3 or 4, wherein the first surfactant comprises polyvinyl alcohol in an amount of 0.35% ± 10% by weight in the water.
6. The method of any one of claims 3-5, wherein the biodegradable poly(lactide) polymer comprises between 10% ± 10% and 15% ± 10% of the organic component.
7. The method of any one of claims 3-6, wherein the solvent comprises a mixture of methylene chloride and ethanol.
8. The method of any one of claims 3-7, wherein the solvent comprises a mixture of methylene chloride and ethanol in a 5:1 volumetric ratio.

9. The method of any one of claims 3-8, wherein the esketamine or ketamine comprises between 3.3% ± 10% and 5.5% ± 10% of the organic component.
10. The method of any one of claims 3-9, wherein the second surfactant comprises polyvinyl alcohol in an amount of 0.35%± 10% to 1.0% ± 10% by weight in the water.
11. The method of any one of claims 3-9, wherein the second surfactant comprises polyvinyl alcohol in an amount of 1.0% ± 10% by weight in water.
12. The method of any one of claims 3-11, wherein a ratio of the continuous phase flow rate to the primary emulsion flow rate is from 66:1 ± 10% to 200:1 ± 10%.

13. The use of the microsphere formulation of claim 1 or 2, in the preparation of a medicament for the treatment of depression.