microangiopathy (TMA), the formation of blood clots in small blood vessels throughout the body, causing a reduction in platelet count (thrombocytopenia) and life-threatening damage to the kidney, brain, heart and other vital organs. Eculizumab (SOLIRIS™, Alexion) has been granted orphan drug designation for the treatment of aHUS in the United States and Europe.

[0006] There is a desire for stable aqueous compositions of an anti-C5 antibody (e.g., eculizumab) that allow long term storage without substantial loss in efficacy.

SUMMARY

[0007] The disclosure provides a stable aqueous composition comprising consisting essentially of, or consisting of (a) about 10 to about 100 mg/ml of an anti-C5 antibody, (b) a surfactant, (c) a stabilizer, and (d) a buffer having a pH of about 5.0 to about 7.8, wherein the stabilizer is trehalose, sucrose, sorbitol, arginine, or a combination thereof.

[0007a] In one aspect, the present disclosure refers to a stable aqueous composition comprising: (a) an anti-C5 antibody, (b) a surfactant, (c) a stabilizer, and (d) a buffer having a pH of 5.0 to 7.8, wherein the stabilizer is trehalose, sucrose, sorbitol, arginine, or a combination thereof; and wherein the composition contains about 10 mg/mL of the anti-C5 antibody.

[0008] The disclosure also provides a stable aqueous composition consisting essentially of (a) about 10 mg/ml of an anti-C5 antibody, (b) about 0.01 to about 0.1% (w/v) of a surfactant, (c) about 1 to about 20 mM buffer having a pH of 5.5 to 7.5, and (d) a stabilizer selected from the group consisting of trehalose, sucrose, sorbitol, arginine, or a combination thereof. Such a composition is suitable for administration (e.g., intravenous administration) to a subject. As such, the disclosure provides a method of treating a disorder in which C5 activity is detrimental in a subject, comprising administering the stable aqueous composition to the subject, thereby treating the disorder in the subject.

[0008a] In another aspect, the present disclosure refers to a stable aqueous composition consisting essentially of: (a) about 10 mg/ml of an anti-C5 antibody, (b) 0.01% to 0.1% (w/v) of a surfactant, (c) 1 to 20 mM buffer having a pH of 5.5 to 7.5, and (d) a stabilizer selected from the group consisting of trehalose, sucrose, sorbitol, arginine, and a combination thereof.

[0008b] In another example, there is provided a stable aqueous composition consisting essentially of: (a) about 30 mg/ml of an anti-C5 antibody, (b) about 0.01% to about 0.1% (w/v) of a surfactant, (c) about 1 mM to about 20 mM buffer having a pH of 5.5 to 7.5, and (d) a stabilizer selected from the group consisting of trehalose, sucrose, sorbitol, arginine, and a combination thereof.

[0009] The disclosure provides a stable aqueous composition consisting essentially of (a) about 50 mg/ml of an anti-C5 antibody, (b) about 0.01 to about 0.1% (w/v) of a surfactant, (c) about 1 to about 20 mM buffer having a pH of 5.5 to 7.5, and (d) a stabilizer selected from the group consisting of trehalose, sucrose, sorbitol, arginine, or a combination thereof. Stable aqueous compositions containing high concentrations (e.g., 50 mg/ml) of the anti-C5 antibody can be useful for storage.

[0009a] In another example, there is provided a stable aqueous composition consisting essentially of: (a) about 50 mg/ml of an anti-C5 antibody, (b) about 0.01% to about 0.1% (w/v) of a surfactant, (c) about 1 mM to about 20 mM buffer having a pH of 5.5 to 7.5, and (d) a stabilizer selected from the group consisting of trehalose, sucrose, sorbitol, arginine, and a combination thereof.

[0009b] In another aspect, the present disclosure refers to a method of preparing a composition suitable for administration comprising diluting the stable aqueous composition as described herein with an anti-C5 antibody to be about 10mg/ml of the antibody when the concentration of antibody is not about 10 mg/mL, in which the stable aqueous composition comprises (a) 0.01% to 0.1% (w/v) of surfactant selected from polysorbate 20 or polysorbate 80, (b) 1 mM to 20 mM buffer selected from phosphate, histidine, or a combination thereof, and (c) a stabilizer selected from the group consisting of trehalose, sucrose, sorbitol, arginine, wherein the concentration of the stabilizer is 1% to 20% (w/v) when the stabilizer is at least one selected from trehalose, sucrose, and sorbitol, and
wherein the concentration of the stabilizer is 50mM to 300mM when the stabilizer is arginine.

DETAILED DESCRIPTION OF THE INVENTION

[0010] The invention provides a stable aqueous composition comprising an anti-C5 antibody, wherein the composition has increased stability relative to conventional anti-C5 antibody formulations even at higher anti-C5 concentrations relative to conventional anti-C5 antibody formulations.

[0011] In particular, the invention provides a stable aqueous composition comprising, consisting essentially of, or consisting of (a) about 10 to about 100 mg/ml of an anti-C5

[0023] In another embodiment, the buffer comprises histidine. The buffer can comprise about 1 mM to about 30 mM (e.g., about 1 mM, about 5 mM, about 10 mM, about 15 mM, about 20 mM, about 25 mM, about 30 mM, or a range between any of these values, such as about 1 mM to about 20 mM) or about 5 mM to about 15 mM (e.g., about 5 mM, about 10 mM, about 15 mM, or a range between any of these values) histidine. In a particular embodiment, the buffer comprises 10 mM histidine.

[0024] The stabilizer is selected from the group consisting of polyol, or amino acid, or a combination thereof. The polyol may be at least one selected from the group consisting of trehalose, sucrose, sorbitol, and mannitol. The amino acid may be arginine. More preferably, the stabilizer may be selected from the group consisting of trehalose, sucrose, sorbitol, arginine, or a combination thereof. In one embodiment, the stabilizer is arginine. In another embodiment, the stabilizer is trehalose. Any suitable amount of the stabilizer can be included in the composition.

[0025] For example, when the stabilizer is trehalose, the composition can comprise about 1% to about 20% (e.g., about 1%, about 1.5%, about 2%, about 2.5%, about 3%, about 3.5%, about 4%, about 4.5%, about 5%, about 5.5%, about 6%, about 6.5%, about 7%, about 7.5%, about 8%, about 8.5%, about 9%, about 9.5%, about 10%, about 10.5%, about 11%, about 11.5%, about 12%, about 12.5%, about 13%, about 13.5%, about 14%, about 14.5%, about 15%, about 15.5%, about 16%, about 16.5%, about 17%, about 17.5%, about 18%, about 18.5%, about 19%, about 19.5%, about 20%, or a range between any of these values) (w/v) or about 7.6% to about 11.4% (e.g., about 7.6%, about 8%, about 8.5%, about 9%, about 9.5%, about 10%, about 10.5%, about 11%, about 11.4%, or a range between any of these values) (w/v) trehalose. In one embodiment, the composition comprises about 9.5% (w/v) trehalose.

[0026] When the stabilizer is sorbitol, the composition can comprise about 1% to about 20% (e.g., about 1%, about 1.5%, about 2%, about 2.5%, about 3%, about 3.5%, about 4%, about 4.5%, about 5%, about 5.5%, about 6%, about 6.5%, about 7%, about 7.5%, about 8%, about 8.5%, about 9%, about 9.5%, about 10%, about 10.5%, about 11%, about 11.5%, about 12%, about 12.5%, about 13%, about 13.5%, about 14%, about 14.5%, about 15%, about 15.5%, about 16%, about 16.5%, about 17%, about 17.5%, about 18%, about 18.5%, about 19%, about 19.5%, about 20%, or a range between any of these values) (w/v) or about 4% to about 6% (e.g., about 4%, about 4.5%, about 5%, about 5.5%, about 6%, or a range between any of these values) (w/v) sorbitol. In one embodiment, the composition comprises about 5% (w/v) sorbitol.

[0027] When the stabilizer is sucrose, the composition can comprise about 1% to about 20% (e.g., about 1%, about 1.5%, about 2%, about 2.5%, about 3%, about 3.5%, about 4%, about 4.5%, about 5%, about 5.5%, about 6%, about 6.5%, about 7%, about 7.5%, about 8%, about 8.5%, about 9%, about 9.5%, about 10%, about 10.5%, about 11%, about 11.5%, about

CLAIMS:

1. A stable aqueous composition comprising:

(a) an anti-C5 antibody,

(b) a surfactant,

(c) a stabilizer, and

(d) a buffer having a pH of 5.0 to 7.8,

wherein the stabilizer is trehalose, sucrose, sorbitol, arginine, or a combination thereof; and

wherein the composition contains about 10 mg/mL of the anti-C5 antibody.

2. The stable aqueous composition of claim 1, wherein the composition does not comprise glycine.

3. The stable aqueous composition of claim 1 or 2, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 1, and a heavy chain comprising the amino acid sequence of SEQ ID NO: 2.

4. The stable aqueous composition of any one of claims 1-3, wherein the antibody is eculizumab.

5. The stable aqueous composition of any one of claims 1-4, wherein the surfactant is 0.01% to 0.1% (w/v) surfactant, and wherein the surfactant is polysorbate 20 or polysorbate 80.

6. The stable aqueous composition of any one of claims 1-5, wherein the buffer is 1 mM to 30mM buffer, and wherein the buffer comprises phosphate, histidine, or a combination thereof.

7. The stable aqueous composition of any one of claims 1-6, wherein the antibody neutralizes human C5 activity with an IC_{50} of 2-4 μg/ml based on an in vitro hemolysis assay.

8. The stable aqueous composition of claim 7, wherein the in vitro hemolysis assay comprises:

(a) diluting the composition,

(b) adding human serum to the diluted composition and incubating with a sample containing red blood cells, and

(c) measuring hemolysis.

9. A stable aqueous composition consisting essentially of:

(a) about 10 mg/ml of an anti-C5 antibody,

(b) 0.01% to 0.1% (w/v) of a surfactant,

(c) 1 to 20 mM buffer having a pH of 5.5 to 7.5, and

(d) a stabilizer selected from the group consisting of trehalose, sucrose, sorbitol, arginine, and a combination thereof.

10. The stable aqueous composition of claim 9, wherein the surfactant is selected from polysorbate 20 or polysorbate 80,

wherein the buffer is selected from phosphate, histidine, or a combination thereof, and wherein the concentration of the stabilizer is 1% to 20% (w/v) when the stabilizer is at least one selected from trehalose, sucrose, and sorbitol,

wherein the concentration of the stabilizer is 50mM to 300mM when the stabilizer is arginine.

11. The stable aqueous composition of claim 9 or 10, wherein the antibody is eculizumab.

12. A method of preparing a composition suitable for administration comprising diluting the stable aqueous composition of any one of claims 1-11 with an anti-C5 antibody to be about 10mg/ml of the antibody when the concentration of antibody is not about 10 mg/mL, in which the stable aqueous composition comprises

(a) 0.01% to 0.1% (w/v) of surfactant selected from polysorbate 20 or polysorbate 80,

(b) 1 mM to 20 mM buffer selected from phosphate, histidine, or a combination thereof, and

(c) a stabilizer selected from the group consisting of trehalose, sucrose, sorbitol, arginine,

wherein the concentration of the stabilizer is 1% to 20% (w/v) when the stabilizer is at least one selected from trehalose, sucrose, and sorbitol, and

wherein the concentration of the stabilizer is 50mM to 300mM when the stabilizer is arginine.