[0005] The presence of tert-butyl alcohol (TBA) in lyophilization formulations has been shown to improve reconstitution time of small quantities or low-doses (*e.g.*, milligram quantities) of biological molecules (See, e.g., U.S. Patent Application Publication No. US 2014/0044717; Nail et al., (2002) J Pharma Sci. Vol. 91; Degobert et al., (2016) Drying Technology; Yong et al., (2009) Int J Pharmaceutics, 371:71-81; Teagarden and Baker (2002) Eur J Pharma Sci 15:115-133; Vessot and Andrieu (2012) Drying Technology (2012) 30:377-385).

[0006] However, the use of TBA in a co-solvent system in lyophilized formulations of biological molecules and its effects on reconstitution time and polypeptide stability has not been well-characterized in polypeptide formulations containing large quantities of protein (*e.g.*, gram quantities) or with high protein concentrations.

[0007] Thus a need exists for methods and formulations of lyophilized biological molecules for large quantities and concentrations (*i.e.*, high-concentration, high-dose) polypeptide compositions, including antibody compositions, which provide reduced or fast reconstitution times as well as maintain integrity and stability of the biological molecule. The present invention meets this need by providing methods and formulations for reducing reconstitution times of lyophilized polypeptides, in which the methods and formulations maintain integrity and stability of the lyophilized polypeptides, in particular for lyophilized antibody compositions of high-concentration and/or high-dose formulations.

SUMMARY

[0008] The present disclosure provides methods and formulations useful for reducing the reconstitution time of lyophilized polypeptides, for example, lyophilized antibody compositions.

[0009] In one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized polypeptide composition, wherein the method comprises preparing a liquid composition comprising the polypeptide, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid polypeptide/TBA mixture, freezing the liquid polypeptide/TBA mixture, lyophilizing the liquid polypeptide/TBA mixture to form a lyophilized polypeptide composition, and reconstituting the lyophilized polypeptide composition with a diluent, wherein the time for reconstituting the polypeptide lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same

polypeptide lyophilized in the absence of TBA. In some examples, the amount of TBA added to the liquid polypeptide composition to form a liquid polypeptide/TBA mixture is between about 0.5% to about 20% by volume. In other examples, the amount of TBA added to the liquid polypeptide composition to form the liquid polypeptide/TBA mixture is selected from the group consisting of 0.5%, 1%, 2.5%, 5%, 7.5%, 10%, 12.5%, 15%, 17.5%, and 20% by volume. In yet other examples, the amount of TBA added to the liquid polypeptide composition to form the liquid polypeptide/TBA mixture is between about 1% to about 20% by volume, about 1% to about 10% by volume, about 1% to about 5% by volume, about 5% to about 20% by volume, or about 5% to about 10% by volume. In one example, the TBA is added to the liquid composition comprising the polypeptide immediately prior to freezing the liquid polypeptide/TBA mixture. In certain examples, the polypeptide is an antibody. In some examples, the polypeptide is an antibody and the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1 prior to adding TBA to the liquid composition.

[0010] In one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized antibody composition, wherein the method comprises preparing a liquid composition comprising the antibody, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid antibody/TBA mixture, freezing the liquid antibody/TBA mixture, lyophilizing the liquid antibody/TBA mixture to form a lyophilized antibody composition, and reconstituting the lyophilized antibody composition with a diluent, wherein the time for reconstituting the antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same antibody lyophilized in the absence of TBA. In some examples, the amount of TBA added to the liquid polypeptide composition to form a liquid polypeptide/TBA mixture is between about 0.5% to about 20% by volume. In other examples, the amount of TBA added to the liquid polypeptide composition to form the liquid polypeptide/TBA mixture is selected from the group consisting of 0.5%, 1%, 2.5%, 5%, 7.5%, 10%, 12.5%, 15%, 17.5%, and 20% by volume. In yet other examples, the amount of TBA added to the liquid polypeptide composition to form the liquid polypeptide/TBA mixture is between about 1% to about 20% by volume, about 1% to about 10% by volume, about 1% to about 5% by volume, about 5% to about 20% by volume, or about 5% to about 10% by volume. In some examples, the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar

ratio of sugar:antibody of at least about 360:1 prior to adding TBA to the liquid composition. In one example, the TBA is added to the liquid composition comprising the polypeptide immediately prior to freezing the liquid polypeptide/TBA mixture. In one example, the antibody is a monoclonal antibody. In one example, the antibody is a human monoclonal antibody. In one example, the antibody is a humanized monoclonal antibody. In one example, the antibody is a chimeric antibody. In one example, the antibody is an antibody fragment. In one example, the antibody is a bispecific antibody. In one example, the antibody is an antibody-drug conjugate (*e.g.*, an immunoconjugate).

[0011] In one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized polypeptide composition, wherein the method comprises preparing a liquid composition comprising the polypeptide, wherein the concentration of the polypeptide in the liquid composition comprising the polypeptide is between about 10 mg/ml to about 150 mg/ml, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid polypeptide/TBA mixture, freezing the liquid polypeptide/TBA mixture, lyophilizing the liquid polypeptide/TBA mixture to form a lyophilized polypeptide composition, and reconstituting the lyophilized polypeptide composition with a diluent, wherein the time for reconstituting the polypeptide lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same polypeptide lyophilized in the absence of TBA. In some examples, the concentration of the polypeptide in the liquid composition comprising the polypeptide is between about 10 mg/ml to about 250 mg/ml, between about 25 mg/ml to about 250 mg/ml, between about 50 mg/ml to about 250 mg/ml, between about 100 mg/ml to about 250 mg/ml, between about 150 mg/mml to about 250 mg/ml, between about 25 mg/ml to about 100 mg/ml, between about 50 mg/ml to about 100 mg/ml, between about 25 mg/ml to about 125 mg/ml, or between about 50 mg/ml to about 125 mg/ml. In some examples, the concentration of the polypeptide in the liquid composition comprising the polypeptide is about 25 mg/ml, about 40 mg/ml, about 50 mg/ml, about 60 mg/ml, about 70 mg/ml, about 100 mg/ml, about 125 mg/ml, about 150 mg/ml, about 200 mg/ml, or about 250 mg/ml. In certain examples, the polypeptide is an antibody. In some examples, the amount of TBA added to the liquid polypeptide composition to form a liquid polypeptide/TBA mixture is between about 0.5% to about 20% by volume. In some examples, the polypeptide is an antibody and the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1 prior to adding TBA to the liquid composition.

[0012] In one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized polypeptide composition, wherein the method comprises preparing a liquid composition comprising the polypeptide, wherein the amount of the polypeptide in the liquid composition comprising the polypeptide is between about 150 mg to about 11 grams, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid polypeptide/TBA mixture, freezing the liquid polypeptide/TBA mixture, lyophilizing the liquid polypeptide/TBA mixture to form a lyophilized polypeptide composition, and reconstituting the lyophilized polypeptide composition with a diluent, wherein the time for reconstituting the polypeptide lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same polypeptide lyophilized in the absence of TBA. In some examples, the amount of the polypeptide in the liquid composition comprising the polypeptide is about 150 mg, about 250 mg, about 500 mg, about 750 mg, about 1 gram, about 2 grams, about 3 grams, about 4 grams, about 5 grams, about 6 grams, about 7 grams, about 8 grams, about 9 grams, about 10 grams, or about 11 grams. In some examples, the amount of the polypeptide in the liquid composition comprising the polypeptide is between about 150 mg to 11 grams. In some examples, the amount of the polypeptide in the liquid composition comprising the polypeptide is between about 150 mg to about 1 gram, between about 500 mg to about 1 gram, between about 500 mg to about 5 grams, between about 1 gram to about 5 grams, between about 1 gram to about 10 grams, or between about 5 grams to about 10 grams. In some examples, the quantity of the polypeptide in the liquid composition comprising the polypeptide is greater than 11 grams. In certain examples, the polypeptide is an antibody. In some examples, the amount of TBA added to the liquid polypeptide composition to form a liquid polypeptide/TBA mixture is between about 0.5% to about 20% by volume. In some examples, the polypeptide is an antibody and the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1 prior to adding TBA to the liquid composition.

[0013] In one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized polypeptide composition, wherein the method comprises preparing a liquid composition comprising the polypeptide, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid polypeptide/TBA mixture, freezing the liquid polypeptide/TBA mixture, lyophilizing the liquid polypeptide/TBA mixture to form a lyophilized polypeptide composition, and reconstituting the lyophilized polypeptide

composition with a diluent, wherein the time for reconstituting the polypeptide lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same polypeptide lyophilized in the absence of TBA, wherein the time for reconstituting the lyophilized polypeptide composition which was lyophilized in the presence of TBA is reduced by about 40% to about 95% compared to the time for reconstituting the same amount of the same polypeptide composition lyophilized in the absence of TBA. In some examples, the time for reconstituting the lyophilized polypeptide composition which was lyophilized in the presence of TBA is reduced by about 50%, about 60%, about 70%, about 80%, about 90%, about 95%, about 50% to about 60%, about 60% to about 70%, about 70% to about 80%, about 80% to about 90%, or about 90% to about 95% compared to the time for reconstituting the same amount of the same polypeptide composition lyophilized in the absence of TBA. In some examples, the polypeptide is an antibody and the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1 prior to adding TBA to the liquid composition.

[0014] In some examples of the present disclosure, the liquid polypeptide/TBA mixture is lyophilized in a vial, a syringe (including dual-chamber syringe), or a cartridge. In some examples, the liquid polypeptide/TBA mixture is lyophilized in a glass vial. In some examples, the vial is a 6cc vial, a 10cc vial, a 15cc vial, a 20cc vial, a 50cc vial, or a 100cc vial. In some examples, the glass vial is a 6cc vial, a 10cc vial, a 15cc vial, a 20cc vial, a 50cc vial, or a 100cc vial. In some examples, the vials have a capacity or fill volume of 0.1ml, 0.3ml, 0.5ml, 1ml, 2ml, 2.5 ml, 5ml, 10ml, 20ml, 25ml, 50ml, or 100ml. In some examples, the glass vials have a capacity or fill volume of 0.1ml, 0.3ml, 0.5ml, 1ml, 2ml, 2.5 ml, 5ml, 10ml, 20ml, 25ml, 50ml, or 100ml.

[0015] In some examples, reconstituting the lyophilized polypeptide composition is performed under conditions in which reconstituting the lyophilized polypeptide composition is performed under a vacuum. In some example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized polypeptide composition, wherein the method comprises preparing a liquid composition comprising the polypeptide, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid polypeptide/TBA mixture, freezing the liquid polypeptide/TBA mixture, lyophilizing the liquid polypeptide/TBA mixture to form a lyophilized polypeptide composition, and reconstituting the lyophilized polypeptide composition with a diluent, wherein the reconstituting the lyophilized polypeptide composition is performed under conditions in which the lyophilized polypeptide

composition is under a vacuum, and further wherein the time for reconstituting the polypeptide lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same polypeptide lyophilized in the absence of TBA. In some examples, the vacuum is a deep vacuum. In some examples, the vacuum is a partial vacuum. In certain examples, the vacuum is less than 100 Torr. In certain examples, the vacuum is less than 50 Torr. In certain examples, the vacuum is between 100 mTorr and 50 Torr. In one example, the vacuum is at 100 mTorr. In some examples, the polypeptide is an antibody and the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1 prior to adding TBA to the liquid composition.

[0016] In some examples, reconstituting the lyophilized polypeptide composition is performed using a shaker, such as a mechanical shaker. In one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized polypeptide composition, wherein the method comprises preparing a liquid composition comprising the polypeptide, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid polypeptide/TBA mixture, freezing the liquid polypeptide/TBA mixture, lyophilizing the liquid polypeptide/TBA mixture to form a lyophilized polypeptide composition, and reconstituting the lyophilized polypeptide composition with a diluent by using a shaker, wherein the time for reconstituting the polypeptide lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same polypeptide lyophilized in the absence of TBA. In some examples, the vial or container is placed on the shaker. In some examples, the polypeptide is an antibody and the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1 prior to adding TBA to the liquid composition.

[0017] In some examples, reconstituting the lyophilized polypeptide composition is performed under conditions in which the lyophilized polypeptide composition is under a vacuum and using a shaker. In one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized polypeptide composition, wherein the method comprises preparing a liquid composition comprising the polypeptide, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid polypeptide/TBA mixture, freezing the liquid polypeptide/TBA mixture, lyophilizing the liquid polypeptide/TBA mixture to form a lyophilized polypeptide composition, and reconstituting the lyophilized polypeptide composition with a diluent by using a shaker, wherein the reconstituting the

lyophilized polypeptide composition is performed under conditions in which the lyophilized polypeptide composition is under a vacuum, and further wherein the time for reconstituting the polypeptide lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same polypeptide lyophilized in the absence of TBA. In some examples, the vacuum is a deep vacuum. In some examples, the vacuum is a partial vacuum. In certain examples, the vacuum is less than 100 Torr. In certain examples, the vacuum is less than 50 Torr. In certain examples, the vacuum is between 100 mTorr and 50 Torr. In one example, the vacuum is at 100 mTorr. In some examples, the polypeptide is an antibody and the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1 prior to adding TBA to the liquid composition.

[0018] The present disclosure provides liquid polypeptide formulations suitable for lyophilization. In some examples, the present disclosure provides liquid polypeptide formulations suitable for lyophilization, wherein the formulation comprises the polypeptide, a diluent, and TBA, wherein the time for reconstituting the polypeptide lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same polypeptide lyophilized in the absence of TBA. In some examples, the amount of TBA in the liquid formulation is between about 0.5-20% by volume. In some examples, the amount of TBA in the liquid formulation is selected from the group consisting of 0.5%, 1%, 2.5%, 5%, 7.5%, 10%, 12.5%, 15%, 17.5%, and 20% by volume. In other examples, the amount of TBA added to the liquid polypeptide composition to form the liquid polypeptide/TBA mixture is between about 1% to about 20% by volume, between about 1% to about 10% by volume, between about 1% to about 5% by volume, between about 5% to about 20% by volume, or between about 5% to about 10% by volume. In one example, the TBA is added to the liquid composition comprising the polypeptide immediately prior to freezing the liquid polypeptide/TBA mixture. In certain examples, the polypeptide is an antibody. In some examples, the polypeptide is an antibody and the formulation further comprises a sugar at a molar ratio of sugar:antibody of at least about 360:1.

[0019] The present disclosure provides a lyophilized polypeptide composition, wherein the lyophilized polypeptide composition is produced by preparing a liquid composition comprising the polypeptide, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid polypeptide/TBA mixture, freezing the liquid polypeptide/TBA mixture, lyophilizing the liquid polypeptide/TBA mixture to form a lyophilized polypeptide

composition, wherein upon reconstitution of the lyophilized polypeptide composition with a diluent, the time for reconstituting the polypeptide lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same polypeptide lyophilized in the absence of TBA. In some examples, the amount of TBA in the liquid formulation is between about 0.5% to about 20% by volume. In some examples, the amount of TBA in the liquid formulation is selected from the group consisting of 0.5%, 1%, 2.5%, 5%, 7.5%, 10%, 12.5%, 15%, 17.5%, and 20% by volume. In other examples, the amount of TBA added to the liquid polypeptide composition to form the liquid polypeptide/TBA mixture is between about 1% to about 20% by volume, between about 1% to about 10% by volume, between about 1% to about 5% by volume, between about 5% to about 20% by volume, or between about 5% to about 10% by volume. In one example, the TBA is added to the liquid composition comprising the polypeptide immediately prior to freezing the liquid polypeptide/TBA mixture. In certain examples, the polypeptide is an antibody. In certain examples, the addition of TBA to the polypeptide formulation has no effect on the integrity or stability of the polypeptide. In some examples, the polypeptide is an antibody and the lyophilized polypeptide composition is produced by preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1 prior to adding TBA to the liquid composition.

[19a] In one aspect, there is provided a method for reducing reconstitution time of a lyophilized antibody composition, the method comprising: (a) preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1, (b) adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid antibody/TBA mixture, wherein the amount of TBA in the liquid antibody/TBA mixture is about 5%-6% by volume, (c) freezing the liquid antibody/TBA mixture, (d) lyophilizing the liquid antibody/TBA mixture to form a lyophilized antibody composition, (e) reconstituting the lyophilized antibody composition with a diluent, wherein the time for reconstituting the antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same antibody lyophilized in the absence of TBA.

[0020] In one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized antibody composition, wherein the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid antibody/TBA mixture, wherein the amount of TBA in the liquid antibody/TBA mixture is between about 5%-20% by volume, freezing the liquid antibody/TBA mixture, lyophilizing the liquid antibody/TBA mixture to form a lyophilized antibody composition, and reconstituting the lyophilized antibody composition with a diluent, wherein the time for reconstituting the antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same antibody lyophilized in the absence of TBA. In some examples, the amount of TBA added to the liquid antibody composition to form the liquid antibody/TBA mixture is selected from the group consisting of 5%, 7.5%, 10%, 12.5%, 15%, 17.5%, and 20% by volume. In some examples, the amount of TBA added to the liquid antibody composition to form the liquid antibody/TBA mixture is about 5%-6% by volume. In yet other examples, the amount of TBA added to

the liquid antibody composition to form the liquid antibody/TBA mixture is between about 5% to about 10% by volume. In one example, the TBA is added to the liquid composition comprising the antibody immediately prior to freezing the liquid antibody/TBA mixture. In certain examples, the antibody is a full length antibody. In one example, the antibody is a monoclonal antibody. In one example, the antibody is a human monoclonal antibody. In one example, the antibody is a humanized monoclonal antibody. In one example, the antibody is a chimeric antibody. In one example, the antibody is an antibody fragment. In one example, the antibody is an antigen-binding fragment, such as a Fv, Fab, Fab', Fab'-SH, $F(ab')_2$; diabodies; linear antibodies; single-chain antibody molecules (*e.g.* scFv); and multispecific antibodies formed from antibody fragments. In one example, the antibody is a bispecific antibody. In one example, the antibody is an antibody-drug conjugate (*e.g.*, an immunoconjugate). In some examples, the sugar is sucrose or trehalose. In certain examples, the addition of TBA to the liquid composition has no effect on the integrity or stability of the antibody.

[0021] In one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized antibody composition, wherein the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1, wherein the concentration of the antibody in the liquid composition comprising the antibody is between about 10 mg/ml to about 250 mg/ml, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid antibody/TBA mixture, wherein the amount of TBA in the liquid antibody/TBA mixture is between about 5%-20% by volume, freezing the liquid antibody/TBA mixture, lyophilizing the liquid antibody/TBA mixture to form a lyophilized antibody composition, and reconstituting the lyophilized antibody composition with a diluent, wherein the time for reconstituting the antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same antibody lyophilized in the absence of TBA. In some examples, the amount of TBA added to the liquid antibody composition to form the liquid antibody/TBA mixture is about 5%-6% by volume. In some examples, the concentration of the antibody in the liquid composition comprising the antibody is between about 25 mg/ml to about 250 mg/ml, between about 50 mg/ml to about 250 mg/ml, between about 100 mg/ml to about 250 mg/ml, between about 150 mg/mml to about 250 mg/ml, between about 25 mg/ml to about 100 mg/ml, between about 50 mg/ml to about 100 mg/ml, between about 25 mg/ml to about 125 mg/ml, or between about 50 mg/ml to about 125 mg/ml. In some examples, the

concentration of the antibody in the liquid composition comprising the antibody is about 25 mg/ml, about 40 mg/ml, about 50 mg/ml, about 60 mg/ml, about 70 mg/ml, about 100 mg/ml, about 125 mg/ml, about 150 mg/ml, about 200 mg/ml, or about 250 mg/ml. In some examples, the sugar is sucrose or trehalose. In certain examples, the addition of TBA to the liquid composition has no effect on the integrity or stability of the antibody.

[0022] In one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized antibody composition, wherein the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1, wherein the amount of the antibody in the liquid composition comprising the antibody is between about 150 mg to about 11 grams, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid antibody/TBA mixture, wherein the amount of TBA in the liquid antibody/TBA mixture is between about 5%-20% by volume, freezing the liquid antibody/TBA mixture, lyophilizing the liquid antibody/TBA mixture to form a lyophilized antibody composition, and reconstituting the lyophilized antibody composition with a diluent, wherein the time for reconstituting the antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same antibody lyophilized in the absence of TBA. In some examples, the amount of TBA added to the liquid antibody composition to form the liquid antibody/TBA mixture is about 5%-6% by volume. In some examples, the amount of the antibody in the liquid composition comprising the antibody is about 150 mg, about 250 mg, about 500 mg, about 750 mg, about 1 gram, about 2 grams, about 3 grams, about 4 grams, about 5 grams, about 6 grams, about 7 grams, about 8 grams, about 9 grams, about 10 grams, or about 11 grams. In some examples, the amount of the antibody in the liquid composition comprising the antibody is between about 150 mg to about 1 gram, between about 500 mg to about 1 gram, between about 500 mg to about 5 grams, between about 1 gram to about 5 grams, between about 1 gram to about 10 grams, or between about 5 grams to about 10 grams. In some examples, the quantity of the antibody in the liquid composition comprising the antibody is greater than 11 grams. In some examples, the sugar is a sucrose or trehalose. In certain examples, the addition of TBA to the liquid composition has no effect on the integrity or stability of the antibody.

[0023] In one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized antibody composition, wherein the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar ratio of

sugar:antibody of at least about 360:1, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid antibody/TBA mixture, wherein the amount of TBA in the liquid antibody/TBA mixture is between about 5%-20% by volume, freezing the liquid antibody/TBA mixture, lyophilizing the liquid antibody/TBA mixture to form a lyophilized antibody composition, and reconstituting the lyophilized antibody composition with a diluent, wherein the time for reconstituting the antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same antibody lyophilized in the absence of TBA, wherein the time for reconstituting the lyophilized antibody composition which was lyophilized in the presence of TBA is reduced by about 40% to about 95% compared to the time for reconstituting the same amount of the same antibody composition lyophilized in the absence of TBA. In some examples, the amount of TBA added to the liquid antibody composition to form the liquid antibody/TBA mixture is about 5%-6% by volume. In some examples, the time for reconstituting the lyophilized antibody composition which was lyophilized in the presence of TBA is reduced by about 40%, by about 50%, about 60%, about 70%, about 80%, about 90%, about 95%, about 50% to about 60%, about 60% to about 70%, about 70% to about 80%, about 80% to about 90%, or about 90% to about 95% compared to the time for reconstituting the same amount of the same antibody composition lyophilized in the absence of TBA. In some examples, the sugar is sucrose or trehalose. In certain examples, the addition of TBA to the liquid composition has no effect on the integrity or stability of the antibody.

[0024] In some examples of the present disclosure, the liquid antibody/TBA mixture is lyophilized in a vial, a syringe (including dual-chamber syringe), or a cartridge. In some examples, the liquid antibody/TBA mixture is lyophilized in a glass vial. In some examples, the vial is a 6cc vial, a 10cc vial, a 15cc vial, a 20cc vial, a 50cc vial, or a 100cc vial. In some examples, the vials have a capacity or fill volume of 0.1ml, 0.3ml, 0.5ml, 1ml, 2ml, 2.5 ml, 5ml, 10ml, 20ml, 25ml, 50ml, or 100ml.

[0025] In some examples, reconstituting the lyophilized antibody composition is performed under conditions in which reconstituting the lyophilized antibody composition is performed under a vacuum. In some example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized antibody composition, wherein the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid antibody/TBA mixture, wherein the amount of TBA in

the liquid antibody/TBA mixture is between about 5%-20% by volume, freezing the liquid antibody/TBA mixture, lyophilizing the liquid antibody/TBA mixture to form a lyophilized antibody composition, and reconstituting the lyophilized antibody composition with a diluent, wherein the reconstituting the lyophilized antibody composition is performed under conditions in which the lyophilized antibody composition is under a vacuum, and further wherein the time for reconstituting the antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same antibody lyophilized in the absence of TBA. In some examples, the amount of TBA added to the liquid antibody composition to form the liquid antibody/TBA mixture is about 5%-6% by volume. In some examples, the vacuum is a deep vacuum. In some examples, the vacuum is a partial vacuum. In certain examples, the vacuum is less than 100 Torr. In certain examples, the vacuum is less than 50 Torr. In certain examples, the vacuum is between 100 mTorr and 50 Torr. In one example, the vacuum is at 100 mTorr.

[0026] In some examples, reconstituting the lyophilized antibody composition is performed using a shaker, such as a mechanical shaker. In one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized antibody composition, wherein the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid antibody/TBA mixture, wherein the amount of TBA in the liquid antibody/TBA mixture is between about 5%-20% by volume, freezing the liquid antibody/TBA mixture, lyophilizing the liquid antibody/TBA mixture to form a lyophilized antibody composition, and reconstituting the lyophilized antibody composition with a diluent by using a shaker, wherein the time for reconstituting the antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same antibody lyophilized in the absence of TBA. In some examples, the vial or container is placed on the shaker. In some examples, the amount of TBA added to the liquid antibody composition to form the liquid antibody/TBA mixture is about 5%-6% by volume.

[0027] In some examples, reconstituting the lyophilized antibody composition is performed under conditions in which the lyophilized antibody composition is under a vacuum and using a shaker. In one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized antibody composition, wherein the method comprises preparing a liquid composition comprising the antibody and a sugar at a molar

ratio of sugar:antibody of at least about 360:1, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid antibody/TBA mixture, wherein the amount of TBA in the liquid antibody/TBA mixture is between about 5%-20% by volume, freezing the liquid antibody/TBA mixture, lyophilizing the liquid antibody/TBA mixture to form a lyophilized antibody composition, and reconstituting the lyophilized antibody composition with a diluent by using a shaker, wherein the reconstituting the lyophilized antibody composition is performed under conditions in which the lyophilized antibody composition is under a vacuum, and further wherein the time for reconstituting the antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same antibody lyophilized in the absence of TBA. In some examples, the vacuum is a deep vacuum. In some examples, the vacuum is a partial vacuum. In certain examples, the vacuum is less than 100 Torr. In certain examples, the vacuum is less than 50 Torr. In certain examples, the vacuum is between 100 mTorr and 50 Torr. In one example, the vacuum is at 100 mTorr. In some examples, the amount of TBA added to the liquid antibody composition to form the liquid antibody/TBA mixture is about 5%-6% by volume.

[0028] The steps of the methods of the present disclosure may be performed by one person or entity, or the steps may be performed by multiple people or by multiple entities. The steps may be performed by multiple people or multiple entities at the direction of one person or one entity. For example, one person or entity may prepare the liquid composition comprising the polypeptide and a sugar, and a different person or entity may add TBA to the liquid composition to form a liquid polypeptide/TBA mixture prior to freezing the liquid polypeptide/TBA mixture. In another example, one person or entity may lyophilize the liquid polypeptide/TBA mixture to form a lyophilized polypeptide composition, and a different person or entity may reconstitute the lyophilized polypeptide composition with a diluent.

[0029] Accordingly, in one example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized polypeptide or antibody composition, wherein the method comprises adding tert-butyl alcohol (TBA) to a liquid composition comprising the polypeptide or antibody and a sugar at a molar ratio of at least about 360:1 to form a liquid polypeptide or antibody/TBA mixture, wherein the amount of TBA in the liquid polypeptide or antibody/TBA mixture is about 5%-20% by volume, freezing the liquid polypeptide or antibody/TBA mixture, lyophilizing the liquid polypeptide or antibody/TBA mixture to form a lyophilized polypeptide or antibody composition, and reconstituting the lyophilized polypeptide or antibody composition with a diluent, wherein the time for reconstituting the

polypeptide or antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same polypeptide or antibody lyophilized in the absence of TBA. In some examples, the amount of TBA in the liquid polypeptide or antibody/TBA mixture is about 5%-6% by volume.

[0030] In another example, the present disclosure provides a method for reducing the reconstitution time of a lyophilized polypeptide or antibody composition, wherein the method comprises adding tert-butyl alcohol (TBA) to a liquid composition comprising the polypeptide or antibody and a sugar at a molar ratio of at least about 360:1 to form a liquid polypeptide or antibody/TBA mixture, wherein the amount of TBA in the liquid polypeptide or antibody/TBA mixture is about 5%-20% by volume, freezing the liquid polypeptide or antibody/TBA mixture, and lyophilizing the liquid polypeptide or antibody/TBA mixture to form a lyophilized polypeptide or antibody composition, wherein the lyophilized polypeptide or antibody composition is subsequently reconstituted with a diluent, wherein the time for reconstituting the polypeptide or antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same polypeptide or antibody lyophilized in the absence of TBA. In some examples, the amount of TBA in the liquid polypeptide or antibody/TBA mixture is about 5%-6% by volume.

[30a] In another aspect, there is provided a liquid antibody formulation suitable for lyophilization, wherein the formulation comprises the antibody, a sugar, a diluent, and TBA, wherein the amount of TBA in the liquid formulation is about 5%-6% by volume, wherein the amount of sugar in the liquid formulation is at a molar ratio of sugar:antibody of at least about 360:1, and wherein the time for reconstituting the antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same antibody lyophilized in the absence of TBA.

[0031] The present disclosure provides liquid antibody formulations suitable for lyophilization. In some examples, the present disclosure provides liquid antibody formulations suitable for lyophilization, wherein the formulation comprises the antibody, a sugar, a diluent, and TBA, wherein the amount of TBA in the liquid formulation is between about 5%-20% by volume, wherein the amount of sugar in the liquid formulation is at a molar ratio of sugar:antibody of at least about 360:1, and wherein the time for reconstituting the antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same antibody lyophilized in the absence of TBA. In some examples, the amount of TBA in the liquid formulation is selected from the group consisting of 5%, 7.5%, 10%, 12.5%, 15%, 17.5%, and 20% by volume. In other examples, the amount of TBA added to the liquid antibody composition to form the liquid antibody/TBA mixture is between about 5% to about 10% by volume. In some examples, the amount of TBA in the liquid formulation is about 5%-6% by volume. In one example, the TBA is added to the liquid composition comprising the antibody immediately prior to freezing the liquid antibody/TBA mixture. In some examples, the

sugar is sucrose or trehalose. In certain examples, the presence of TBA in the liquid antibody formulation has no effect on the integrity or stability of the antibody.

[31a] In another aspect, there is provided a lyophilized antibody composition, wherein the lyophilized antibody composition is produced by preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid antibody/TBA mixture, wherein the amount of TBA in the liquid formulation is about 5%-6% by volume, freezing the liquid antibody/TBA mixture, lyophilizing the liquid antibody/TBA mixture to form a lyophilized antibody composition, wherein upon reconstitution of the lyophilized antibody composition with a diluent, the time for reconstituting the antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same antibody lyophilized in the absence of TBA.

[0032] The present disclosure provides a lyophilized antibody composition, wherein the lyophilized antibody composition is produced by preparing a liquid composition comprising the antibody and a sugar at a molar ratio of sugar:antibody of at least about 360:1, adding tert-butyl alcohol (TBA) to the liquid composition to form a liquid antibody/TBA mixture, wherein the amount of TBA in the liquid antibody/TBA mixture is between about 5%-20% by volume, freezing the liquid antibody/TBA mixture, lyophilizing the liquid antibody/TBA mixture to form a lyophilized antibody composition, wherein upon reconstitution of the lyophilized antibody composition with a diluent, the time for reconstituting the antibody lyophilized in the presence of TBA is less than the time for reconstituting the same amount of the same antibody lyophilized in the absence of TBA. In some examples, the amount of TBA in the liquid formulation is selected from the group consisting of 5%, 7.5%, 10%, 12.5%, 15%, 17.5%, and 20% by volume. In other examples, the amount of TBA added to the liquid antibody composition to form the liquid antibody/TBA mixture is between about 5% to about 10% by volume. In some examples, the amount of TBA added to the liquid antibody composition to form the liquid antibody/TBA mixture is between about 5% to about 6% by volume. In one example, the TBA is added to the liquid composition comprising the antibody immediately prior to freezing the liquid antibody/TBA mixture. In some examples, the sugar is sucrose or trehalose. In certain examples, the addition of TBA to the liquid composition has no effect on the integrity or stability of the antibody in the liquid composition or in the lyophilized antibody composition.

BRIEF DESCRIPTION OF THE DRAWINGS

[0033] Figure 1 sets forth data showing reconstitution times for a lyophilized antibody formulation containing 0%, 0.5%, 1%, 5%, and 20% (v/v) tert-butyl alcohol.

[0034] Figure 2 sets forth data showing reconstitution times for a 2.5 ml lyophilized antibody formulation containing 0%, 5%, and 10% (v/v) tert-butyl alcohol lyophilized in 6cc vials.

[0035] Figure 3 sets forth data showing reconstitution times for a 25 ml lyophilized antibody formulation containing 0%, 1%, 5%, 10%, and 20% (v/v) tert-butyl alcohol lyophilized in 50cc vials.