SUMMARY

[0008] In a first aspect, the present disclosure refers to a method of reducing oxidation of an antibody in an aqueous formulation comprising adding an amount of N-acetyltryptophan to the formulation that prevents oxidation of the antibody, wherein the antibody comprises at least one tryptophan residue with a solvent-accessible surface area (SASA) of greater than about 80$Å^2$. In a second aspect, the present disclosure refers to a method of reducing oxidation of an antibody in an aqueous formulation comprising adding an amount of N-acetyltryptophan to the formulation that prevents oxidation of the antibody, wherein the antibody comprises at least one tryptophan residue with a solvent-accessible surface area (SASA) of greater than about 30%. In a third aspect, the present disclosure refers to a method of reducing oxidation of an antibody in an aqueous formulation comprising determining the SASA values of tryptophan residues in the antibody and adding an amount of N-acetyltryptophan to the formulation that prevents oxidation of the antibody if at least one tryptophan residue has a solvent-accessible surface area (SASA) of greater than about 80$Å^2$. In some examples, the SASA value of the tryptophan residues in calculated by molecular dynamic simulation.

[0009] In some examples, the N-acetyltryptophan is added to the formulation to a concentration of about 0.1 mM to about 5 mM. In some examples, the N-acetyltryptophan is added to the formulation to a concentration of about 0.1 mM to about 1 mM. In some examples, the N-acetyltryptophan is added to the formulation to a concentration about 0.3 mM.

[0010] In some examples, the oxidation of the polypeptide is reduced by about 50%, 75%, 80%, 85%, 90%, 95% or 99%. In some examples, the formulation is stable at about 2 °C to about 8 °C for about 1095 days.

[0011] In some examples, the protein concentration in the formulation is about 1 mg/mL to about 250 mg/mL. In some examples, the formulation has a pH of about 4.5 to about 7.0. In some examples, the formulation further comprises one or more excipients selected from the group consisting of a stabilizer, a buffer, a surfactant, and a tonicity agent.

[0012] In some examples, the formulation is a pharmaceutical formulation suitable for administration to a subject. In some examples, the protein is an antibody. In some examples, the antibody is a polyclonal antibody, a monoclonal antibody, a humanized antibody, a human antibody, a chimeric antibody, a multispecific antibody, or an antibody fragment.

[0013] In a fourth aspect, there is provided a liquid formulation comprising an antibody and an amount of N-acetyltryptophan to prevent oxidation of the antibody,

wherein the antibody has at least one tryptophan residue with a SASA of greater than about 80Å^2. In some examples, the N-acetyltryptophan is added to the formulation to a concentration of about 0.1 mM to about 5 mM. In some examples, the N-acetyltryptophan is added to the formulation to a concentration of about 0.1 mM to about 1 mM. In some examples, the N-acetyltryptophan is added to the formulation to a concentration about 0.3 mM. In some examples, the oxidation of the polypeptide is reduced by about 50%, 75%, 80%, 85%, 90%, 95% or 99%. In some examples, the formulation is stable at about 2 °C to about 8 °C for about 1065 days.

[0014] In some examples, the protein concentration in the formulation is about 1 mg/mL to about 250 mg/mL. In some examples, the formulation has a pH of about 4.5 to about 7.0. In some examples, the formulation further comprises one or more excipients selected from the group consisting of a stabilizer, a buffer, a surfactant, and a tonicity agent.

[0015] In some examples, the formulation is a pharmaceutical formulation suitable for administration to a subject. In some examples, the protein is an antibody. In some examples, the antibody is a polyclonal antibody, a monoclonal antibody, a humanized antibody, a human antibody, a chimeric antibody, a multispecific antibody, or an antibody fragment.

[0016] The present disclosure also refers to a method for screening a formulation for reduced oxidation of a polypeptide wherein the polypeptide comprises at least one tryptophan residue with a SASA of greater than about 80Å^2, the method comprising adding an amount of N-acetyltryptophan to an aqueous composition comprising the polypeptide, adding 2,2'-azobis (2-aminopropane) dihydrochloride (AAPH) to the composition, incubating the composition comprising the polypeptide, N-acetyltryptophan and AAPH for about 14 hours at about 40 °C, measuring the polypeptide for oxidation of tryptophan residues in the polypeptide, wherein a formulation comprising an amount of N-acetyltryptophan that results in no more than about 20% oxidation of tryptophan residues of the polypeptide is a suitable formulation for reduced oxidation of the polypeptide. In some examples, the N-acetyltryptophan and AAPH are incubated for less than about any of 10 hours, 11 hours, 12 hours, 14 hours, 16 hours, 20 hours, or 24 hours. In some examples, no more than about any of 15%, 20% 25%, 30%, or 35%, oxidation of tryptophan residues of the polypeptide is a suitable formulation for reduced oxidation of the polypeptide.

[0017] The present disclosure further refers to a method for screening a formulation for reduced oxidation of a polypeptide comprising determining the SASA values of tryptophan residues in the polypeptide, wherein a tryptophan residue with a SASA of greater than about

80Å2, is subject to oxidation, adding an amount of N-acetyltryptophan to an aqueous composition comprising the polypeptide, adding 2,2'-azobis (2-aminopropane) dihydrochloride (AAPH) to the composition, incubating the composition comprising the polypeptide, N-acetyltryptophan and AAPH for about 14 hours at about 40 °C, measuring the polypeptide for oxidation of tryptophan residues in the polypeptide, wherein a formulation comprising an amount of N-acetyltryptophan that results in no more than about 20% oxidation of tryptophan residues of the polypeptide is a suitable formulation for reduced oxidation of the polypeptide.

[0018] In some examples of the above aspects, the SASA value of the tryptophan residues in calculated by molecular dynamic simulation.

[0019] In a fifth aspect, the present disclosure refers to a kit comprising the liquid formulation of the fourth aspect. In sixth aspect, the present disclosure refers to an article of manufacture comprising the liquid formulation of the fourth aspect.

[0020] Provided herein are formulations comprising a protein and N-acetyl-tryptophan (NAT), and methods of making and using the formulations.

[0021] In some examples, the liquid formulation is a pharmaceutical formulation suitable for administration to a subject. In some examples, the formulation is aqueous.

[0022] In some examples, the NAT prevents oxidation of tryptophan in the protein.

[0023] In some examples, the protein in the formulation is susceptible to oxidation. In some examples, tryptophan in the protein is susceptible to oxidation. In some examples, the protein is an antibody (e.g., a polyclonal antibody, a monoclonal antibody, a humanized antibody, a human antibody, a chimeric antibody, or antibody fragment). In some examples, the protein concentration in the formulation is about 1 mg/mL to about 250 mg/mL.

[0024] In some examples, the formulation further comprises one or more excipients selected from the group consisting of a stabilizer, a buffer, a surfactant, and a tonicity agent. In some examples, the formulation has a pH of about 4.5 to about 7.0.

[0025] The present disclosure refers to a method to determine if a polypeptide in a liquid formulation comprises a tryptophan residue susceptible to oxidation, the method comprising calculating one or more molecule descriptors based on the amino acid sequence of the polypeptide for each tryptophan residue in the polypeptide and applying the one or more molecule descriptors to a machine learning algorithm trained on the one or more molecule descriptors to predict tryptophan oxidation, wherein the molecule descriptors include one or

more of the following: a) number of aspartic acid sidechain oxygens within 7Å of tryptophan delta carbon, b) sidechain solvent accessible surface area (SASA), c) delta carbon SASA, d) total positive charge within 7Å of tryptophan delta carbon, e) backbone SASA, f) tryptophan sidechain angles, g) packing density within 7Å of tryptophan delta carbon, h) tryptophan backbone angles, i) SASA of pseudo-pi orbitals, j) backbone flexibility, or k) total negative charge within 7Å of tryptophan delta carbon. In some examples, two, three, four, five, six, seven, eight, nine, ten or eleven molecule descriptors are used. In some examples, the molecule descriptors comprise the following: a) number of aspartic acid sidechain oxygens within 7Å of tryptophan delta carbon, b) sidechain solvent accessible surface area (SASA), c) delta carbon SASA, d) total positive charge within 7Å of tryptophan delta carbon, e) backbone SASA, f) tryptophan sidechain angles, and g) packing density within 7Å of tryptophan delta carbon. In some examples, oxidation of greater than 35% of tryptophan residues at a particular site indicates susceptibility to oxidation. In some examples, the protein is an antibody. In some examples, the antibody is a polyclonal antibody, a monoclonal antibody, a humanized antibody, a human antibody, a chimeric antibody, a multispecific antibody, or an antibody fragment.

[0026] In some examples, the machine learning algorithm was trained by matching molecule descriptors from molecular dynamic simulations of polypeptides based on amino acid sequence of the polypeptide with experimental data for each tryptophan residue in the polypeptide. In some examples, the one or more molecule descriptors are calculated using a computer.

[0027] The present disclosure also refers to a method to reduce oxidation of a polypeptide, comprising identifying tryptophan residues susceptible to oxidation according to the method as described herein and introducing an amino acid substitution in the polypeptide to replace one or more tryptophan residues susceptible to oxidation with amino acid residues that are not subject to oxidation. The present disclosure refers to a method to reduce oxidation of a polypeptide, comprising introducing an amino acid substitution in the polypeptide to replace one or more tryptophan residues susceptible to oxidation, wherein the one or more tryptophan residues susceptible to oxidation was identified by the method as described herein. In some examples, the tryptophan residue is replaced by an amino acid residue selected from the group consisting of tyrosine, phenylalanine, leucine, isoleucine, alanine, and valine.

[0028] The present disclosure further refers to a method to reduce oxidation of a polypeptide in an aqueous formulation, comprising determining the presence of one or more tryptophan residues in the polypeptide susceptible to oxidation according to the method as described herein, and adding an effective amount of an anti-oxidation agent to the aqueous formulation comprising a polypeptide having a one or more tryptophan residues susceptible to oxidation. The present disclosure also refers to a method to reduce oxidation of a polypeptide in an aqueous formulation, comprising adding an amount of an anti-oxidation agent to the aqueous formulation to prevent oxidation, wherein polypeptide comprises one or more tryptophan residues susceptible to oxidation identified by the method as described herein. In some examples, the anti-oxidation agent is N-acetyltryptophan. In some examples, the N-acetyltryptophan is added to the formulation to a concentration of about 0.1 mM to about 5 mM. In some examples, the N-acetyltryptophan is added to the formulation to a concentration of about 0.1 mM to about 1 mM. In some examples, the N-acetyltryptophan is added to the formulation to a concentration about 0.3 mM. In some examples, the oxidation of the polypeptide is reduced by about 50%, 75%, 80%, 85%, 90%, 95% or 99%. In some examples, the formulation is stable at about 2 °C to about 8 °C for about 1095 days. In some examples, the protein concentration in the formulation is about 1 mg/mL to about 250 mg/mL. In some examples, the formulation has a pH of about 4.5 to about 7.0. In some examples, the formulation further comprises one or more excipients selected from the group consisting of a stabilizer, a buffer, a surfactant, and a tonicity agent. In some examples, the formulation is a pharmaceutical formulation suitable for administration to a subject. In some examples, the protein is an antibody. In some examples, the antibody is a polyclonal antibody, a monoclonal antibody, a humanized antibody, a human antibody, a chimeric antibody, a multispecific antibody, or an antibody fragment.

[0029] The present disclosure also refers to a liquid formulation comprising a polypeptide and an amount of N-acetyltryptophan to prevent oxidation of the polypeptide, wherein the polypeptide has at least one tryptophan residue susceptible to oxidation as measured by the method as described herein. In some examples, the N-acetyltryptophan is added to the formulation to a concentration of about 0.1 mM to about 5 mM. In some examples, the N-acetyltryptophan is added to the formulation to a concentration of about 0.1 mM to about 1 mM. In some examples, the N-acetyltryptophan is added to the formulation to a

concentration about 0.3 mM. In some examples, the oxidation of the polypeptide is reduced by about 50%, 75%, 80%, 85%, 90%, 95% or 99%. In some examples, the formulation is stable at about 2 °C to about 8 °C for about 1065 days. In some examples, the protein concentration in the formulation is about 1 mg/mL to about 250 mg/mL. In some examples, the formulation has a pH of about 4.5 to about 7.0. In some examples, the formulation further comprises one or more excipients selected from the group consisting of a stabilizer, a buffer, a surfactant, and a tonicity agent. In some examples, the formulation is a pharmaceutical formulation suitable for administration to a subject. In some examples, the protein is an antibody. In some examples, the antibody is a polyclonal antibody, a monoclonal antibody, a humanized antibody, a human antibody, a chimeric antibody, a multispecific antibody, or an antibody fragment. In some examples, there is provided a kit comprising the liquid formulation. In some examples, there is provided an article of manufacture comprising the liquid formulation.

[0030] The present disclosure also refers to a method for screening a formulation for reduced oxidation of a polypeptide wherein the polypeptide comprises at least one tryptophan susceptible to oxidation identified by the method as described herein, the method comprising adding an amount of N-acetyltryptophan to an aqueous composition comprising the polypeptide, adding 2,2'-azobis (2-aminopropane) dihydrochloride (AAPH) to the composition, incubating the composition comprising the polypeptide, N-acetyltryptophan and AAPH for about 14 hours at about 40 °C, measuring the polypeptide for oxidation of tryptophan residues in the polypeptide, wherein a formulation comprising an amount of N-acetyltryptophan that results in no more than about 20% oxidation of tryptophan residues of the polypeptide is a suitable formulation for reduced oxidation of the polypeptide. The present disclosure further refers to a method for screening a formulation for reduced oxidation of a polypeptide comprising a) identifying a polypeptide comprising one or more tryptophan residues susceptible to oxidation by the method as described herein, b) adding an amount of N-acetyltryptophan to an aqueous composition comprising the polypeptide identified in step a), c) adding 2,2'-azobis (2-aminopropane) dihydrochloride (AAPH) to the composition, d) incubating the composition comprising the polypeptide, N-acetyltryptophan and AAPH for about 14 hours at about 40 °C, e) measuring the polypeptide for oxidation of tryptophan residues in the polypeptide, wherein a formulation comprising an amount of N-acetyltryptophan that results

in no more than about 20% oxidation of tryptophan residues of the polypeptide is a suitable formulation for reduced oxidation of the polypeptide. The present disclosure refers to a kit comprising the liquid formulation described above. The present disclosure also refers to an article of manufacture comprising the liquid formulation described above.

[0031] The present disclosure further refers to a method for measuring N-acetyl tryptophan (NAT) degradation in a composition comprising N-acetyl tryptophan, the method comprising a) applying the composition to a reverse phase chromatography material, wherein the composition is loaded onto the chromatography material equilibrated in a solution comprising a mobile phase A and a mobile phase B, wherein mobile phase A comprises acid in water and mobile phase B comprises acid in acetonitrile, b) eluting the composition from the reverse phase chromatography material with a solution comprising mobile phase A and mobile phase B wherein the ratio of mobile phase B to mobile phase A is increased compared to step a), wherein NAT degradants elute from the chromatography separately from intact NAT, c) quantifying the NAT degradants and the intact NAT. In some examples, the ratio of mobile phase B to mobile phase A in step a) is about 2:98. In some examples, the ratio of mobile phase B to mobile phase A in step b) increases linearly. In some examples, the ratio of mobile phase B to mobile phase A in step b) increases stepwise. In some examples, the flow rate of the chromatography is about 1.0 mL/minute. In some examples, the ratio of mobile phase B to mobile phase A is increased to about 30:70. In some examples, the ratio of mobile phase B to mobile phase A is increased to about 30:70 in about 16 minutes. In some examples, the ratio of mobile phase B to mobile phase A is further increased to about 90:70. In some examples, the ratio of mobile phase B to mobile phase A is further increased to about 90:70 in about 18.1 minutes. In some examples, the ratio of mobile phase B to mobile phase A is increased to about 26:74. In some examples, the ratio of mobile phase B to mobile phase A is increased to about 26:74 in about 14 minutes. In some examples, the ratio of mobile phase B to mobile phase A is further increased to about 90:70. In some examples, the ratio of mobile phase B to mobile phase A is further increased to about 90:70 in about 16.5 minutes. In some examples, mobile phase A comprises about 0.1% acid in water. In some examples, mobile phase B comprises about 0.1% acid in acetonitrile. In some examples, the acid is formic acid. In some examples, the reverse phase chromatography material comprises a C18 moiety. In some examples, the reverse phase chromatography material comprises a solid support. In some examples, the solid support comprises silica. In some examples, the reverse phase chromatography material is contained in a column. In some examples, the reverse phase chromatography material is a high performance liquid chromatography (HPLC) material or an ultra-high performance liquid chromatography

(UPLC) material. In some examples, NAT and NAT degradation products are detected by absorbance at 240 nm. In some examples, NAT degradation products are identified by mass spectrometry. In some examples, the concentration of NAT in the composition is about 10 nM to about 1 mM. In some examples, NAT degradation products include one or more of N-Ac-(H, 1,2,3,3a,8,8a-hexahydro- 3a-hydroxypyrrolo [2,3-b]-indole 2-carboxylic acid) (N-Ac-PIC), N-Ac- oxyindolylalanine (N-Ac-Oia), N-Ac- N-formyl-kynurenine (N-Ac-NFK), N-Ac- kynurenine (N-Ac-Kyn) and N-Ac-2a,8a-dihydroxy-PIC.

[0032] The present disclosure refers to a method for measuring N-acetyl tryptophan (NAT) degradation in a composition comprising N-acetyl tryptophan and a polypeptide, the method comprising a) diluting the composition with about 8 M guanidine, b) removing the polypeptide from the composition, c) applying the composition to a reverse phase chromatography material, wherein the composition is loaded onto the chromatography material equilibrated in a solution comprising a mobile phase A and a mobile phase B, wherein mobile phase A comprises acid in water and mobile phase B comprises acid in acetonitrile, d) eluting the composition from the reverse phase chromatography material with a solution comprising mobile phase A and mobile phase B wherein the ratio of mobile phase B to mobile phase A is increased compared to step a), wherein NAT degradants elute from the chromatography separately from intact NAT, e) quantifying the NAT degradants and the intact NAT. In some examples, the composition is diluted in about 8M guanidine such that the final concentration of NAT in the composition ranges from about 0.05 mM to about 0.2 mM. In some examples, the composition is diluted in about 8M guanidine such that the final concentration of polypeptide in the composition is less than or equal to about 25 mg/mL. In some examples, the polypeptide is removed from the composition by filtration. In some examples, the filtration uses a filtration membrane with a molecular weight cut-off of about 30 kDal. In some examples, the ratio of mobile phase B to mobile phase A in step a) is about 2:98. In some examples, the ratio of mobile phase B to mobile phase A in step b) increases linearly. In some examples, the ratio of mobile phase B to mobile phase A in step b) increases stepwise. In some examples, the flow rate of the chromatography is about 1.0 mL/minute. In some examples, the ratio of mobile phase B to mobile phase A is increased to about 30:70. In some examples, the ratio of mobile phase B to mobile phase A is increased to about 30:70 in about 16 minutes. In some examples, the ratio of mobile phase B to mobile phase A is further increased to about 90:70. In some examples, the ratio of mobile phase B to mobile phase A is further increased to about 90:70 in about 18.1 minutes. In some examples, the ratio of mobile

phase B to mobile phase A is increased to about 26:74. In some examples, the ratio of mobile phase B to mobile phase A is increased to about 26:74 in about 14 minutes. In some examples, the ratio of mobile phase B to mobile phase A is further increased to about 90:70. In some examples, the ratio of mobile phase B to mobile phase A is further increased to about 90:70 in about 16.5 minutes. In some examples, mobile phase A comprises about 0.1% acid in water. In some examples, mobile phase B comprises about 0.1% acid in acetonitrile. In some examples, the acid is formic acid. In some examples, the reverse phase chromatography material comprises a C18 moiety. In some examples, the reverse phase chromatography material comprises a solid support. In some examples, the solid support comprises silica. In some examples, the reverse phase chromatography material is contained in a column. In some examples, the reverse phase chromatography material is a high performance liquid chromatography (HPLC) material or an ultra-high performance liquid chromatography (UPLC) material. In some examples, NAT and NAT degradation products are detected by absorbance at 240 nm. In some examples, NAT degradation products are identified by mass spectrometry. In some examples, the concentration of NAT in the composition is about 0.1 mM to about 5 mM. In some examples, the concentration of NAT in the composition is about 0.3 mM. In some examples, NAT degradation products include one or more of N-Ac-PIC, N-Ac-Oia, N-Ac-NFK, N-Ac-Kyn and N-Ac-2a,8a-dihydroxy-PIC.

[0033] In some examples of the above aspects, the protein concentration in the formulation is about 1 mg/mL to about 250 mg/mL. In some examples, the formulation has a pH of about 4.5 to about 7.0. In some examples, the formulation further comprises one or more excipients selected from the group consisting of a stabilizer, a buffer, a surfactant, and a tonicity agent. In some examples, the formulation is a pharmaceutical formulation suitable for administration to a subject. In some examples, the polypeptide is an antibody. In some examples, the antibody is a polyclonal antibody, a monoclonal antibody, a humanized antibody, a human antibody, a chimeric antibody, a multispecific antibody or antibody fragment.

[0034] The present disclosure refers to a method to monitor degradation of NAT in a composition comprising measuring the degradation of NAT in a sample of the composition according to the methods as described herein, wherein the method is repeated one or more times. In some examples, the method is repeated every month, every two months, every four months or every six months.

[0035] The present disclosure also refers to a quality assay for a pharmaceutical composition, the quality assay comprising measuring degradation of NAT in a sample of the pharmaceutical composition according to the methods as described herein, wherein the amount of NAT degradants measured in the composition determines if the pharmaceutical composition is suitable for administration to an animal. In some examples, an amount of NAT degradants in the pharmaceutical composition of less than about 10 ppm indicates that the pharmaceutical composition is suitable for administration to the animal.

[0036] It is to be understood that one, some, or all of the properties of the various examples described herein may be combined to form other examples of the present disclosure. These and other aspects of the disclosure will become apparent to one of skill in the art. These and other examples of the disclosure are further described by the detailed description that follows.

BRIEF DESCRIPTION OF THE DRAWINGS

[0037] **FIG. 1** shows the protection from AAPH stress-induced oxidation of various tryptophan residues by NAT in proteins Mab2, Mab4, Mab1, and Mab6. Both graphs present the same data, differing in x-axis scale. The legend includes the *in silico*-calculated solvent-accessible surface area for each residue tested.

[0038] **FIGS. 2**A and **2**B show the relationship between tryptophan oxidation by AAPH and % sidechain SASA. **FIG. 2**A shows results from a data set including 38 IgG1 mAbs. **FIG. 2**B shows results from a data set including 121 mAbs across diverse frameworks including IgG1, IgG2, IgG4, and murine.

[0039] **FIG. 3** shows random decision forest accuracy as a function of the number of estimators used during training.

[0040] **FIG. 4** shows random decision forest accuracy as a function of the number of features considered during training.

[0041] **FIG. 5** shows random decision forest accuracy as a function of the tree depth used during training.

[0042] **FIG. 6** shows the feature importance (gini importance) of the 14 most relevant simulation-based molecule descriptors for an optimized random decision forest. Training parameters included: 5000 estimators, 3 features considered per node, and a tree depth of 10.

[0043] **FIG. 7** shows potential degradants of NAT (b series), along with the corresponding Trp degradants (a series).

[0044] **FIG. 8A** shows reverse phase chromatograms 0.2 mM NAT after subjection to different stress conditions. Starred peaks represent peaks only observed under ICH light stress. **FIG. 8B** shows

CLAIMS

What is claimed is:

1. A method of reducing oxidation of an antibody in an aqueous formulation comprising adding an amount of N-acetyltryptophan to the formulation that prevents oxidation of the antibody, wherein the antibody comprises at least one tryptophan residue with a solvent-accessible surface area (SASA) of greater than about 80$Å^2$.

2. A method of reducing oxidation of an antibody in an aqueous formulation comprising adding an amount of N-acetyltryptophan to the formulation that prevents oxidation of the antibody, wherein the antibody comprises at least one tryptophan residue with a solvent-accessible surface area (SASA) of greater than about 30%.

3. A method of reducing oxidation of an antibody in an aqueous formulation comprising determining the SASA values of tryptophan residues in the antibody and adding an amount of N-acetyltryptophan to the formulation that prevents oxidation of the antibody if at least one tryptophan residue has a solvent-accessible surface area (SASA) of greater than about 80$Å^2$.

4. The method of claim 3, wherein the SASA value of the tryptophan residues is calculated by molecular dynamic simulation.

5. The method of any one of claims 1-4, wherein the N-acetyltryptophan is added to the formulation to a concentration of about 0.1 mM to about 5 mM;

wherein optionally the N-acetyltryptophan is added to the formulation to a concentration of about 0.1 mM to about 1 mM;

wherein optionally the N-acetyltryptophan is added to the formulation to a concentration about 0.3 mM;

wherein optionally the oxidation of the antibody is reduced by about 50%, 75%, 80%, 85%, 90%, 95% or 99%;

wherein optionally the formulation is stable at about 2 ℃ to about 8 ℃ for about 1095 days;

wherein optionally the antibody concentration in the formulation is about 1 mg/mL to about 250 mg/mL;

wherein optionally the formulation has a pH of about 4.5 to about 7.0;

wherein optionally the formulation further comprises one or more excipients selected from the group consisting of a stabilizer, a buffer, a surfactant, and a tonicity agent;

wherein optionally the formulation is a pharmaceutical formulation suitable for administration to a subject; and

wherein optionally the antibody is a polyclonal antibody, a monoclonal antibody, a humanized antibody, a human antibody, a chimeric antibody, a multispecific antibody, or an antibody fragment.

6. A liquid formulation comprising an antibody and an amount of N-acetyltryptophan to prevent oxidation of the antibody, wherein the antibody has at least one tryptophan residue with a SASA of greater than about 80$Å^2$.

7. The liquid formulation of claim 6, wherein the N-acetyltryptophan is added to the formulation to a concentration of about 0.1 mM to about 5 mM;

wherein optionally the N-acetyltryptophan is added to the formulation to a concentration of about 0.1 mM to about 1 mM;

wherein optionally the N-acetyltryptophan is added to the formulation to a concentration about 0.3 mM;

wherein optionally the oxidation of the antibody is reduced by about 50%, 75%, 80%, 85%, 90%, 95% or 99%;

wherein optionally the formulation is stable at about 2 °C to about 8 °C for about 1065 days;

wherein optionally the antibody concentration in the formulation is about 1 mg/mL to about 250 mg/mL;

wherein optionally the formulation has a pH of about 4.5 to about 7.0;

wherein optionally the formulation further comprises one or more excipients selected from the group consisting of a stabilizer, a buffer, a surfactant, and a tonicity agent;

wherein optionally the formulation is a pharmaceutical formulation suitable for administration to a subject; and

wherein optionally the antibody is a polyclonal antibody, a monoclonal antibody, a humanized antibody, a human antibody, a chimeric antibody, a multispecific antibody, or an antibody fragment.

8. A kit comprising the liquid formulation of claim 6 or 7.

9. An article of manufacture comprising the liquid formulation of claim 6 or 7.

10. The method of claim 5, wherein the N-acetyltryptophan is added to the formulation to a concentration of about 0.1 mM to about 1 mM.