BRIEF SUMMARY

[0005] In some examples, provided is a method of reducing a hydrolytic enzyme activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising: a capture step; one or more ion exchange (IEX) chromatography steps; and a depth filtration step, thereby reducing the hydrolytic enzyme activity rate of the composition as compared to purification of the sample without the depth filtration step.

[0005a] In one aspect, the disclosure provides a method of reducing a hydrolytic enzyme activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in order: a capture step; a CEX chromatography step; AEX chromatography step; a depth filtration step; a virus filtration step; and an ultrafiltration/diafiltration (UF/DF) step, thereby reducing the hydrolytic enzyme activity rate of the composition as compared to purification of the sample without the depth filtration step.

[0006] In some examples, each of the one or more IEX chromatography steps is selected from the group consisting of: an anion exchange (AEX) chromatography step, a cation exchange (CEX) chromatography step, and a multimodal ion exchange (MMIEX) chromatography step. In some examples, the MMIEX chromatography step comprises a multimodal cation exchange/ anion exchange (MM-AEX/CEX) chromatography step.

[0007] In some examples, the method further comprises a virus filtration step.

[0008] In some examples, the method further comprises an ultrafiltration/diafiltration (UF/DF) step.

[0009] In some examples, the purification platform comprises, in order: the capture step; the CEX chromatography step; the AEX chromatography step; the depth filtration step; the virus filtration step; and the UF/DF step.

[0010] In some examples, the depth filtration step comprises processing via a depth filter, and wherein the depth filter is a X0SP depth filter, a C0SP depth filter, a D0SP depth filter, or an EMPHAZE™ depth filter.

[0011] In some examples, the method further comprises a HIC step comprising processing via Sartobind® phenyl.

[0012] In other examples, provided is a method of reducing a hydrolytic enzyme activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising: a capture step; a multimodal hydrophobic interaction/ ion exchange (MM-HIC/IEX) chromatography step; and a hydrophobic interaction chromatography

[0022] In some examples, the purification platform comprises, in order: the capture step; the MM-HIC/AEX chromatography step; the depth filtration step; and the HIC step. In some examples, the depth filtration step comprises processing via a depth filter, and wherein the depth filter is a X0SP depth filter, a C0SP depth filter, or a D0SP depth filter. In some examples, the depth filtration step comprises processing via a depth filter, and the depth filter is an EMPHAZE™ depth filter. In some examples, the MM-HIC/ AEX chromatography step comprises processing via Capto™ Adhere or Capto™ Adhere ImpRes.

[0023] In other examples, provided is a method of reducing a hydrolytic enzyme activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising: a capture step; one or more ion exchange (IEX) chromatography steps; and a hydrophobic interaction chromatography (HIC) step, thereby reducing the hydrolytic enzyme activity rate of the composition as compared to purification of the sample without the HIC step.

[0024] In some examples, the one or more IEX chromatography steps is a cation exchange (CEX) chromatography step.

[0025] In some examples, the method further comprises a virus filtration step.

[0026] In some examples, the method further comprises an ultrafiltration/diafiltration (UF/DF) step.

[0027] In some examples, the method further comprises a depth filtration step performed at any stage prior to the UF/DF step.

[0028] In some examples, the purification platform comprises, in order: the capture step; the CEX chromatography step; the HIC step; the virus filtration step; and the UF/DF step.

[0029] In other examples, provided is a method of reducing a hydrolytic enzyme activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising: one or more ion exchange (IEX) chromatography steps; a hydrophobic interaction chromatography (HIC) step; and a depth filtration step, thereby reducing the hydrolytic enzyme activity rate of the composition as compared to purification of the sample

without the HIC step or the depth filtration step. In some examples, the reduction is as compared to purification of the sample without the HIC and the depth filtration step.

[0030] In some examples, each of the one or more IEX chromatography steps is selected from the group consisting of: an anion exchange (AEX) chromatography step, a cation exchange (CEX) chromatography step, and a multimodal ion exchange (MMIEX) chromatography step. In some examples, the MMIEX chromatography step comprises a multimodal cation exchange/ anion exchange (MM-AEX/CEX) chromatography step.

[0031] In some examples, the method further comprises an ultrafiltration/diafiltration (UF/DF) step.

[0032] In some examples, the purification platform comprises, in order: the CEX chromatography step; the HIC step; the MMIEX chromatography step; the AEX chromatography step; the depth filter step; and the UF/DF step.

[0033] In other examples, provided is a method of reducing a hydrolytic enzyme activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising: a capture step; one or more ion exchange (IEX) chromatography steps; a multimodal hydrophobic interaction/ ion exchange (MM-HIC/IEX) chromatography steps; and one or both of: a hydrophobic interaction chromatography (HIC) step; and a depth filtration step, thereby reducing the hydrolytic enzyme activity rate of the composition as compared to purification of the sample without the HIC step or the depth filtration step.

[0034] In some examples, the reduction is as compared to purification of the sample without the HIC and the depth filtration step.

[0035] In some examples, the method further comprises a virus filtration step.

[0036] In some examples, the method further comprises an ultrafiltration/diafiltration (UF/DF) step.

[0037] In some examples, the depth filtration step is performed as a load filter for the MM-HIC/IEX chromatography step, as a load filter for the HIC step, or following the HIC step.

[0052] In other examples, provided is a pharmaceutical composition obtained from a method described herein.

[0053] In other examples, provided is a formulated antibody moiety composition comprising an antibody moiety and a polysorbate, wherein the composition has a reduced rate of polysorbate hydrolysis, wherein the shelf-life of the composition is more than 12 months.

[0054] In other examples, provided is a formulated antibody moiety composition comprising an antibody moiety and a polysorbate, wherein the composition has a reduced rate of polysorbate hydrolysis activity, wherein the shelf-life of the composition is extended compared to the shelf-life indicated in documents filed with a health authority related to the formulated antibody moiety composition, wherein the shelf-life is extended by at least 3 months compared to the shelf-life indicated in said documents.

[0055] In some examples, the rate of polysorbate hydrolysis is reduced by at least about 20%.

[0056] In other examples, provided is a formulated antibody moiety composition comprising an antibody moiety, wherein the formulated antibody moiety composition has a reduced degradation of polysorbate, wherein the degradation is reduced by at least about 20% compared to the degradation indicated in documents filed with a health authority related to the formulated antibody moiety composition.

[0057] In other examples, provided is a formulated antibody moiety composition comprising an antibody moiety and a polysorbate, wherein the polysorbate is degraded during storage of the liquid composition by 50% or less per year.

[0058] In some examples, the antibody moiety is a monoclonal antibody. In some examples, the antibody moiety is a human, humanized, or chimeric antibody. In some examples, the antibody is selected from the group consisting of an anti-TAU antibody, an anti-TGFβ3 antibody, an anti-VEGF-A antibody, an anti-CD20 antibody, an anti-CD40 antibody, an anti-HER2 antibody, an anti-IL6 antibody, an anti-IgE antibody, an anti-IL13 antibody, an anti-TIGIT antibody, an anti-PD-L1 antibody, an anti-VEGF-A/ANG2 antibody, an anti-CD79b antibody, an anti-ST2 antibody, an anti-factor D antibody, an anti-factor IX antibody, an anti-factor

CLAIMS

What is claimed is:

1. A method of reducing a hydrolytic enzyme activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in order:

    a capture step;

    a CEX chromatography step;

    AEX chromatography step;

    a depth filtration step;

    a virus filtration step; and

    an ultrafiltration/diafiltration (UF/DF) step,

    thereby reducing the hydrolytic enzyme activity rate of the composition as compared to purification of the sample without the depth filtration step.

2. The method of claim 1, wherein the depth filtration step comprises processing via a depth filter, and wherein the depth filter is a X0SP depth filter, a C0SP depth filter, a D0SP depth filter, a Polisher ST depth filter, or an EMPHAZE™ depth filter.

3. The method of claim 1 or 2, further comprising a HIC step comprising processing via Sartobind® phenyl.

4. The method of any one of claims 1-3, wherein the capture step comprises processing via affinity chromatography.

5. The method of any one of claims 1-4, wherein the capture step is performed in a bind-and-elute mode.

6. The method of claim 4 or 5, wherein the affinity chromatography is selected from the group consisting of a protein A chromatography, a protein G chromatography, a protein A/G chromatography, a FcXL chromatography, a protein XL chromatography, a kappa chromatography, and a kappaXL chromatography.

7. The method of any one of claims 1-6, wherein the depth filtration step comprises processing via a depth filter.

8. The method of claim 7, wherein the depth filter is used as a load filter.

9. The method of claim 7 or 8, wherein the depth filter comprises a substrate comprising one or more of a diatomaceous earth composition, a silica composition, a cellulose fiber, a polymeric fiber, a cohesive resin, and an ash composition.

10. The method of claim 9, wherein at least a portion of the substrate of the depth filter comprises a surface modification.

11. The method of claim 10, wherein the surface modification is one or more of a quaternary amine surface modification, a cationic surface modification, and an anionic surface modification.

12. The method of any one of claims 7-11, wherein the depth filter is selected from the group consisting of: a X0SP depth filter, a D0SP depth filter, a C0SP depth filter, an EMPHAZE™ depth filter, a PDD1 depth filter, a PDE1 depth filter, a PDH5 depth filter, a ZETA PLUS™ 120ZA depth filter, a ZETA PLUS™ 120ZB depth filter, a ZETA PLUS™ DELI depth filter, a ZETA PLUS™ DELP depth filter, and a Polisher ST depth filter.

13. The method of claim 12, wherein

the depth filter is the X0SP depth filter, the D0SP depth filter, or the C0SP depth filter, and wherein the processing via the depth filter is performed at a pH of 4.5 to 8, or

wherein the depth filter is the EMPHAZE™ depth filter, and wherein processing via the depth filter is performed at a pH of 7 to 9.5, or

wherein the depth filter is the Polisher ST depth filter, and wherein processing via the depth filter is performed at a pH of 4.5 to 9.

14. The method of any one of claims 1-13, wherein each of the CEX and AEX chromatography steps comprises processing via an ion exchange (IEX) chromatography membrane or an IEX chromatography column.

15. The method of claim 14, wherein the IEX chromatography membrane or the IEX chromatography column is selected from the group consisting of: SPSFF, QSFF, SPXL, Streamline™ SPXL, ABx™, Poros™ XS, Poros™ 50HS, DEAE, DMAE, TMAE, QAE, and MEP-Hypercel™.

16. The method of any one of claims 1-15, wherein the purification platform is for purification of a target from the sample, and wherein the sample comprises the target and one or more host cell impurities.

17. The method of claim 16, wherein the target comprises a polypeptide, preferably the target is an antibody moiety.

18. The method of claim 17, wherein the antibody moiety is a monoclonal antibody, preferably the antibody moiety is a human, humanized, or chimeric antibody.

19. The method of claim 17 or 18, wherein the antibody moiety is selected from the group consisting of: an anti-TAU antibody, an anti-TGFβ3 antibody, an anti-VEGF-A antibody, an anti-CD20 antibody, an anti-CD40 antibody, an anti-HER2 antibody, an anti-IL6 antibody, an anti-IgE antibody, an anti-IL13 antibody, an anti-TIGIT antibody, an anti-PD-L1 antibody, an anti-VEGF-A/ANG2 antibody, an anti-CD79b antibody, an anti-ST2 antibody, an anti-factor D antibody, an anti-factor IX antibody, an anti-factor X antibody, an anti-abeta antibody, an anti-CEA antibody, an anti-CEA/CD3 antibody, an anti-CD20/CD3 antibody, an anti-FcRH5/CD3 antibody, an anti-Her2/CD3 antibody, an anti-FGFR1/KLB antibody, a FAP-4-1 BBL fusion protein, a FAP-IL2v fusion protein, and a TYRP1 TCB antibody.

20. The method of any one of claims 16-19, wherein the one or more host cell impurities comprises a host cell protein, preferably, the host cell protein is a hydrolytic enzyme, and

more preferably, the hydrolytic enzyme is a lipase, an esterase, a thioesterase, a phospholipase, carboxylesterase, hydrolase, cutinase, or a ceramidase.

21. The method of any one of claims 1-20, wherein the sample comprises a host cell or components originating therefrom.

22. The method of any one of claims 1-21, wherein the sample is, or is derived from, a cell culture sample.

23. The method of claim 22, wherein the cell culture sample comprises a host cell, and wherein the host cell is a Chinese hamster ovary (CHO) cell or an *E. coli* cell.

24. The method of any one of claims 1-23, further comprising a sample processing step.

25. The method of any one of claims 1-24, wherein the reduction in the hydrolytic enzyme activity rate is at least 20%.

26. The method of any one of claims 1-25, further comprising determining the hydrolytic enzyme activity rate of the composition and/or determining the level of one or more hydrolytic enzymes in the composition.

27. The method of any one of claims 1-26, wherein the composition comprises a polysorbate, preferably the polysorbate is selected from the group consisting of polysorbate 20, polysorbate 40, polysorbate 60, and polysorbate 80.