reducing the enzymatic hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

[0005a] In one aspect, the present disclosure refers to a method of reducing an enzymatic polysorbate hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order: (a) a capture step; and (b) a depth filtration step, wherein the depth filtration step comprises processing via a depth filter, and wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite, wherein the depth filter is a PDD1 depth filter, thereby reducing the enzymatic polysorbate hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

[0006] In some examples, the enzymatic hydrolysis activity rate is an enzymatic polysorbate hydrolysis activity rate. In some examples, the relative reduction of the enzymatic hydrolysis activity rate of the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least about 20%.

[0006a] In one aspect, the present disclosure refers to a method of reducing the level of one or more hydrolytic enzymes in a composition obtained from a purification platform, wherein the one or more hydrolytic enzymes are capable of hydrolyzing a polysorbate, the method comprising subjecting a sample to the purification platform comprising, in the following order: (a) a capture step; and (b) a depth filtration step, wherein the depth filtration step comprises processing via a depth filter, and wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite, wherein the depth filter is a PDD1 depth filter, thereby reducing the level of the hydrolytic enzyme in the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

[0007] In another example, the present disclosure refers to a method of reducing the level of one or more hydrolytic enzymes in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising: (a) a capture step; and (b) a depth filtration step, thereby reducing the level of the hydrolytic enzyme in the composition as compared to purification of the sample using the same purification platform without the depth filtration step. In some examples, the one or more hydrolytic enzymes are capable of hydrolyzing a polysorbate. In some examples, the relative reduction of the level of one or more hydrolytic enzymes in the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least about 20%.

[0007a] In one aspect, the present disclosure refers to a method for reducing degradation of a polysorbate in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order: (a) a capture step; and (b) a depth filtration step, wherein the depth filtration step comprises processing via a depth filter, and wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite, wherein the depth filter is a PDD1 depth filter, thereby reducing degradation of the polysorbate in the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

[0008] In another example, the present disclosure refers to a method for reducing degradation of a polysorbate in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising: (a) a capture step; and (b) a depth filtration step, thereby reducing degradation of the polysorbate in the composition as compared to purification of the sample using the same purification platform without the depth filtration step. In some examples, the relative reduction of degradation of the polysorbate in the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least about 5%.

[0009] In some examples, the purification platform is for purification of a target from the sample, wherein the sample comprises the target and one or more host cell impurities. In some examples, the target comprises a polypeptide. In some examples, the host cell impurity is a host cell protein.

[0010] In some examples, the depth filtration step is performed prior to the capture step, or the depth filtration step is performed after the capture step.

[0017] In some examples, the purification platform further comprises a hydrophobic interaction chromatography (HIC) purification step. In some examples, the HIC purification step is performed prior to, in between, or after the one or more purification steps, if present. In some examples, the HIC purification step is performed after the one or more purification steps and prior to the UFDF step, if present.

[0018] In some examples, the purification platform further comprises a pH hold step, wherein the pH hold step is performed after the one or more purification steps, if present, and prior to the UFDF step.

[0019] In some examples, the purification platform further comprises a virus filtration step, wherein the virus filtration step is performed after the pH hold step and prior to the UFDF step. In some examples, the virus filtration step comprises processing via a virus filter.

[0020] In some examples, the HIC purification step comprises processing via a HIC filter.

[0021] In some examples, the one or more purification steps each independently comprise processing via a chromatography selected from the group consisting of: ion exchange chromatography, anion exchange chromatography, cation exchange chromatography, a hydrophobic charge induction chromatography, a ceramic hydroxyapatite chromatography, and a multimodal chromatography. In some examples, the one or more purification steps each independently comprise processing via a chromatography selected from the group consisting of: DEAE, DMAE, TMAE, QAE, SPSFF, SPXL, QSFF, MEP-Hypercel™, Capto MMC, and Capto Adhere.

[0021a] In one aspect, the present disclosure refers to a method of reducing an enzymatic polysorbate hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order: (a) a capture step comprising processing via affinity chromatography; (b) a virus inactivation step; (c) a depth filtration step; (d) a second polypeptide purification step; (e) a third polypeptide purification step; and (f) a ultrafiltration/diafiltration (UFDF) step, wherein the depth filtration step comprises processing via a depth filter, and wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite, wherein the depth filter is a PDD1 depth filter, thereby reducing the enzymatic polysorbate hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

[0022] In another example, the present disclosure refers to a method of reducing an enzymatic hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order: (a) a capture step comprising processing via affinity chromatography; (b) a virus inactivation step; (c) a second polypeptide purification step; (d) a third polypeptide purification step; and (e) a ultrafiltration/diafiltration (UFDF) step, wherein the purification platform further comprises a depth filtration step performed at one or more of the following: (i) prior to the capture step; (ii) after the capture step and prior to the virus inactivation step; (iii) after the virus inactivation step and prior to the second polypeptide purification step; (iv) after the second polypeptide purification step and prior to the third polypeptide purification step; or (v) after the third polypeptide purification step and prior to the ultrafiltration/diafiltration (UFDF) step; thereby reducing the enzymatic hydrolysis activity rate of

the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

[0023] In some examples, the purification platform further comprises, in the following order, a pH hold step and a virus filtration step performed after the third polypeptide purification step and prior to the UFDF step. In some examples, the virus filtration step comprises processing via a virus filter.

[0024] In some examples, the purification platform further comprises a hydrophobic interaction chromatography (HIC) purification step performed at one or more of the following: (i) after the third polypeptide purification step and prior to the pH hold step; (ii) after the pH hold step and prior to the virus filtration step; or (iii) after the virus filtration step and prior to the UFDF step.

[0024a] In one aspect, the present disclosure refers to a method of reducing an enzymatic polysorbate hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order: (a) a first depth filtration step; (b) a capture step comprising processing via affinity chromatography; (c) a virus inactivation step; and (d) a second depth filtration step; wherein the second depth filtration step comprises processing via a depth filter, and wherein the depth filter of the second depth filtration step comprises cellulose fibers, diatomaceous earth, and perlite, wherein the depth filter of the second depth filtration step is a PDD1 depth filter, thereby reducing the enzymatic polysorbate hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the second depth filtration step.

[0025] In some examples, the method further comprises determining the enzymatic hydrolysis activity rate of the composition.

[0026] In some examples, the method further comprises determining the level of one or more hydrolytic enzymes in the composition.

[0027] In some examples, the composition comprises a polysorbate. In some examples, the polysorbate is selected from the group consisting of polysorbate 20, polysorbate 40, polysorbate 60, and polysorbate 80.

[0028] In some examples, the method further comprises comprising a sample processing step.

[0029] In some examples, the sample is, or is derived from, a cell culture sample. In some examples, 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. In some examples, the sample comprises a host cell or components originating therefrom. In some examples, the sample comprises one or more host cell proteins, and wherein one of the one or more host cell proteins is a hydrolytic enzyme.

[0030] In some examples, the hydrolytic enzyme is a lipase, an esterase, a thioesterase, a phospholipase, or a ceramidase.

[0031] In some examples, the sample comprises a target, and wherein the target is an antibody moiety. In some examples, the antibody moiety is a monoclonal antibody. In some examples, the antibody moiety is a human, humanized, or chimeric antibody.

CLAIMS

What is claimed is:

1. A method of reducing an enzymatic polysorbate hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order:

(a) a capture step; and

(b) a depth filtration step,

wherein the depth filtration step comprises processing via a depth filter, and

wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite,

wherein the depth filter is a PDD1 depth filter,

thereby reducing the enzymatic polysorbate hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

2. The method of claim 1, wherein the relative reduction of the enzymatic polysorbate hydrolysis activity rate of the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least 20%.

3. A method of reducing the level of one or more hydrolytic enzymes in a composition obtained from a purification platform, wherein the one or more hydrolytic enzymes are capable of hydrolyzing a polysorbate, the method comprising subjecting a sample to the purification platform comprising, in the following order:

(a) a capture step; and

(b) a depth filtration step,

wherein the depth filtration step comprises processing via a depth filter, and

wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite,

wherein the depth filter is a PDD1 depth filter,

thereby reducing the level of the hydrolytic enzyme in the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

4. The method of claim 3, wherein the relative reduction of the level of one or more hydrolytic enzymes in the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least 20%.

5. A method for reducing degradation of a polysorbate in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order:

(a) a capture step; and

(b) a depth filtration step,

wherein the depth filtration step comprises processing via a depth filter, and

wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite,

wherein the depth filter is a PDD1 depth filter,

thereby reducing degradation of the polysorbate in the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

6. The method of claim 5, wherein the relative reduction of degradation of the polysorbate in the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least 5%.

7. The method of any one of claims 1-6, wherein the purification platform is for purification of a target from the sample, wherein the sample comprises the target and one or more host cell impurities.

8. The method of claim 7, wherein the target comprises a polypeptide.

9. The method of claim 7 or 8, wherein the host cell impurity is a host cell protein.

10. The method of any one of claims 1-9, wherein the capture step comprises processing via affinity chromatography.

11. The method of claim 10, 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 protein L chromatography, a FcXL chromatography, a protein XL chromatography, a kappa chromatography, and a kappaXL chromatography.

12. The method of any one of claims 1-11, wherein the purification platform further comprises a virus inactivation step, wherein the virus inactivation step is performed after the capture step.

13. The method of claim 12, wherein the depth filtration step is performed after the virus inactivation step.

14. The method of any one of claims 1-13, wherein the purification platform further comprises a second depth filtration step performed prior to the capture step.

15. The method of claim 14, wherein the second depth filtration step comprises processing via a second depth filter.

16. The method of claim 15, wherein the second 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.

17. The method of claim 16, wherein at least a portion of the substrate of the second depth filter comprises a surface modification.

18. The method of claim 17, wherein the surface modification is one or more of a quaternary amine surface modification, a cationic surface modification, and an anionic surface modification.

19. The method of any one of claims 1-18, wherein the purification platform further comprises a sterilization step performed prior to the capture step and, if present, after the second depth filtration step, wherein the sterilization step comprises processing via a sterile filter.

20. The method of any one of claims 1-19, wherein the purification platform further comprises one or more purification steps, and wherein the one or more purification steps is performed after the capture step, the depth filtration step, and, if present, the virus inactivation step.

21. The method of claim 20, wherein the one or more purification steps comprise polypeptide purification steps.

22. The method of claim 20 or 21, wherein the purification platform further comprises another depth filtration step performed prior to, in between, or after the one or more purification steps.

23. The method of any one of claims 1-22, wherein the purification platform further comprises an ultrafiltration/diafiltration (UFDF) step, and wherein the UFDF step is performed after the one or more purification steps.

24. The method of claim 23, wherein the purification platform further comprises another depth filtration step performed prior to or after the UFDF step.

25. The method of any one of claims 1-24, wherein the purification platform further comprises a hydrophobic interaction chromatography (HIC) purification step.

26. The method of claim 25, wherein the HIC purification step is performed prior to, in between, or after the one or more purification steps, if present.

27. The method of claim 25, wherein the HIC purification step is performed after the one or more purification steps and prior to the UFDF step, if present.

28. The method of claim 23 or 24, wherein the purification platform further comprises a pH hold step, wherein the pH hold step is performed after the one or more purification steps, if present, and prior to the UFDF step.

29. The method of claim 28, wherein the purification platform further comprises a virus filtration step, wherein the virus filtration step is performed after the pH hold step and prior to the UFDF step.

30. The method of claim 29, wherein the virus filtration step comprises processing via a virus filter.

31. The method of claim 25, wherein the HIC purification step comprises processing via a HIC filter.

32. The method of any one of claims 20-31, wherein the one or more purification steps each independently comprise processing via a chromatography selected from the group consisting of: ion exchange chromatography, anion exchange chromatography, cation exchange chromatography, a hydrophobic charge induction chromatography, a ceramic hydroxyapatite chromatography, and a multimodal chromatography.

33. The method of any one of claims 20-32, wherein the one or more purification steps each independently comprise processing via a chromatography selected from the group consisting of: DEAE; DMAE; TMAE; QAE; crosslinked, beaded-form of agarose; quaternary amine, crosslinked, beaded-form of agarose; and mercaptoethylpyridine (MEP).

34. A method of reducing an enzymatic polysorbate hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order:

(a) a capture step comprising processing via affinity chromatography;
(b) a virus inactivation step;
(c) a depth filtration step;
(d) a second polypeptide purification step;
(e) a third polypeptide purification step; and
(f) a ultrafiltration/diafiltration (UFDF) step,
wherein the depth filtration step comprises processing via a depth filter, and
wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite,
wherein the depth filter is a PDD1 depth filter,

thereby reducing the enzymatic polysorbate hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

35. The method of claim 34, wherein the purification platform further comprises, in the following order, a pH hold step and a virus filtration step performed after the third polypeptide purification step and prior to the UFDF step.

36. The method of claim 35, wherein the virus filtration step comprises processing via a virus filter.

37. The method of claim 35 or 36, wherein the purification platform further comprises a hydrophobic interaction chromatography (HIC) purification step performed at one or more of the following:

(i) after the third polypeptide purification step and prior to the pH hold step;

(ii) after the pH hold step and prior to the virus filtration step; or

(iii) after the virus filtration step and prior to the UFDF step.

38. A method of reducing an enzymatic polysorbate hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order:

(a) a first depth filtration step;

(b) a capture step comprising processing via affinity chromatography;

(c) a virus inactivation step; and

(d) a second depth filtration step;

wherein the second depth filtration step comprises processing via a depth filter, and

wherein the depth filter of the second depth filtration step comprises cellulose fibers, diatomaceous earth, and perlite, wherein the depth filter of the second depth filtration step is a PDD1 depth filter,

thereby reducing the enzymatic polysorbate hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the second depth filtration step.

39. The method of claim 38, wherein the first depth filtration step comprises processing via a depth filter.

40. The method of claim 39, wherein the depth filter of the first depth filtration step 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.

41. The method of claim 40, wherein at least a portion of the substrate of the depth filter of the first depth filtration step comprises a surface modification.

42. The method of claim 41, wherein the surface modification is one or more of a quaternary amine surface modification, a cationic surface modification, and an anionic surface modification.

43. The method of any one of claims 38-42, wherein the purification platform further comprises a sterilization step performed after the first depth filtration step and prior to the capture step, wherein the sterilization step comprises processing via a sterile filter.

44. The method of any one of claims 1-43, wherein the depth filter comprising cellulose fibers, diatomaceous earth, and perlite comprises two layers.

45. The method of any one of claims 1-44, further comprising determining the enzymatic polysorbate hydrolysis activity rate of the composition.

46. The method of any one of claims 1-45, further comprising determining the level of one or more hydrolytic enzymes in the composition.

47. The method of any one of claims 1-46, wherein the composition comprises a polysorbate.

48. The method of claim 47, wherein the polysorbate is selected from the group consisting of polysorbate 20, polysorbate 40, polysorbate 60, and polysorbate 80.

49. The method of any one of claims 1-48, further comprising a sample processing step.

50. The method of any one of claims 1-49, wherein the sample is, or is derived from, a cell culture sample.

51. The method of claim 50, 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.

52. The method of any one of claims 1-51, wherein the sample comprises a host cell or components originating therefrom.

53. The method of any one of claims 1-52, wherein the sample comprises one or more host cell proteins, and wherein one of the one or more host cell proteins is a hydrolytic enzyme.

54. The method of claim 53, wherein the hydrolytic enzyme is a lipase, an esterase, a thioesterase, a phospholipase, or a ceramidase.

55. The method of any one of claims 1-54, wherein the sample comprises a target, and wherein the target is an antibody moiety.

56. The method of claim 55, wherein the antibody moiety is a monoclonal antibody.

57. The method of claim 55 or 56, wherein the antibody moiety is a human, humanized, or chimeric antibody.

58. The method of any one of claims 55-57, wherein the antibody moiety is selected from the group consisting of 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 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-tau 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.

59. The method of any one of claims 55-58, wherein the antibody moiety is selected from the group consisting of ocrelizumab, pertuzumab, trastuzumab, tocilizumab, faricimab, polatuzumab, gantenerumab, cibisatamab, crenezumab, mosunetuzumab, tiragolumab,

bevacizumab, rituximab, atezolizumab, obinutuzumab, lampalizumab, lebrikizumab, omalizumab, ranibizumab, emicizumab, selicrelumab, prasinezumab, RO6874281, and RO7122290.

60. The method of any one of claims 1-59, wherein the shelf-life of the composition is more than 24 months.

61. The method of any one of claims 1-60, wherein the shelf-life of the composition is extended by at least 6 months compared to a shelf-life of a composition obtained from purification of the sample using the same purification platform without the depth filter comprising cellulose fibers, diatomaceous earth, and perlite.