

square meter of a virus filter membrane costs about 3000 EUR in average and a cell culture medium is used costing about 10 EUR per liter medium, then the costs for 1000L virus filtered media are 13 EUR per liter medium, which increases the costs of goods for media preparation by about 30%. If 2000L can be filtered with a virus filter membrane then the costs decrease to 11.50 EUR. Further increase of volumetric capacities, e.g. beyond 5000 L reduces the costs to less than 0.6 EUR per liter medium, which makes the additional costs for providing a virus filtered medium considerably low. As a result, the high costs of using virus filters, in particular in upstream decontamination of potential viral or viral contamination decreases significantly by increasing the volumetric capacity of the virus filtration method.

[0010] The present invention fully addresses this problem of high costs and low volumetric capacity of virus filters, respectively. The volumetric capacity of the virus filter can be increased by performing the virus filtration for at least about 24 hours through a virus filter having an effective pore size of maximum 75 nm. Surprisingly, it has been found that the volumetric capacity of the used costly virus filters can be better exploited leading to a 2 to 100-fold increase of the volumetric capacity while maintaining the filter integrity. Although a 2 to 3-fold increase of volumetric capacity already has a great impact to the production process and the related production costs, with the method according to the invention an up to 100-fold increase of volumetric capacity or even more can be achieved. This offers great opportunities and makes viral removal cost efficient even with costly virus filters that now can be used to further improve viral safety in cell culture processes, in particular in upstream viral removal of cell culture processes, pharmaceutical, diagnostic and/or cosmetic and food processes.

SUMMARY

[0011] In one aspect, there is provided a method for removing a viral contaminant from a preparation, said preparation being a cell culture media-medium or at least a component of a cell culture media-medium, comprising the step of: a) ~~S~~subjecting said preparation to filtration for at

least about 24 hours through a virus filter having an effective pore size of maximum 75 nm, wherein the filtration operates at a volumetric capacity of at least about 2000 L/m².

[0012] In one aspect, there is provided use of a virus filter having an effective pore size of maximum 75 nm in a filtration for at least about 24 hours for the removal of viral contaminant from a preparation, said preparation being a cell culture media medium or at least a one component of a cell culture media medium, wherein the filtration operates at a volumetric capacity of at least about 2000 L/m².

[0013] ~~In one aspect, there is provided~~Also disclosed is the use of a preparation, being a cell culture media or at least a component of a cell culture media obtainable according to any method of the present disclosure for cell culture; pharmaceutical, diagnostic and/or cosmetic preparations as well as in food preparations.

[0014] All methods and uses according to the disclosure can operate at a volumetric capacity of at least about 2000 L/m², preferably at least about 3000 L/m², most preferably at least about 5000 L/m². In addition, the preparation is subjected to filtration and the filtration is performed, respectively, for at least 24 hours or for at least about 48 hours up to about 7 months or about 72 hours up to about 3 months. The filtration is performed at a temperature from about 2 °C to about 60 °C, or about 10 to about 40 °C, preferably about 15 to about 37°C.

[0015] In all embodiments of the disclosure filtration is performed at a pressure ranging from about 100 mbar to about 4000 mbar, preferably from about 200 mbar to about 3500 mbar, most preferably from about 1000 mbar to about 3000 mbar.

[0016] In all embodiments of the disclosure the used virus filter achieves at least a 1Log₁₀ reduction value (LRV) for a viral contaminant.

[0017] Surprisingly, it has been found that the volumetric capacity of virus filters can be enormously increased when operating the filtration process for at least about 24 hours. Normally, preparations for cell culture e.g. bulk cell culture media or buffers are filtered batchwise within about 2 to about 10 hours after preparation of the bulk preparations in order to avoid contamination of the preparations by bacterial or viral growth. It has turned out that in practice the maximum capacity of the used virus filters is not nearly exploited in filtration processes filtering the respective preparations within a timeframe of about 2 to about 10 hours. Therefore excessive

CLAIMS

1. A method for removing a viral contaminant from a preparation, said preparation being a cell culture medium or at least a component of a cell culture medium, comprising subjecting said preparation to filtration for at least about 24 hours through a virus filter having an effective pore size of maximum 75 nm, wherein the filtration operates at a volumetric capacity of at least about 2000 L/m².
2. The method of claim 1, wherein the filtration operates at a volumetric capacity of at least about 3000 L/m².
3. The method of claim 2, wherein the filtration operates at a volumetric capacity of at least about 5000 L/m².
4. The method of any one of claims 1-3, wherein said preparation is subjected to filtration for at least about 48 hours up to about 7 months.
5. The method of claim 4, wherein said preparation is subjected to filtration for at least about 72 hours up to about 3 months.
6. The method of any one of claims 1-5, further comprising feeding the filtrate to a cell culture or to at least one component of a cell culture medium.
7. The method of any one of claims 1-6, wherein the filtration is a continuous filtration.
8. The method of any one of claims 1-7, wherein filtration is performed at a temperature from about 2 °C to about 60 °C.
9. The method of claim 8, wherein the filtration is performed at a temperature from about 10

°C to about 40 °C.

10. The method of claim 9, wherein the filtration is performed at a temperature from about 15 °C to about 37°C.

11. The method of any one of claims 1-10, wherein said virus filter achieves at least a 1 Log₁₀ reduction value (LRV) for a viral contaminant.

12. The method of claim 11, wherein said virus filter achieves at least a 4 LRV for a viral contaminant.

13. The method of claim 12, wherein said virus filter achieves at least a 6 LRV for a viral contaminant.

14. The method of any of claims 1-13 where filtration is performed using two or more filters arranged in series, in parallel or a mixture of both.

15. The method of claim 14, wherein filtration is performed using two filters arranged in parallel in a system of tubes comprising a Y-shaped junction and wherein each filter is in fluid communication with a branch of the Y-shaped junction and a preparation supply source.

16. The method of any of claims 1-15, wherein filtration is performed at a pressure ranging from about 100 mbar to about 4000 mbar.

17. The method of claim 16, wherein the filtration is performed at a pressure ranging from about 100 mbar to about 3500 mbar.

18. The method of claim 17, wherein the filtration is performed at a pressure ranging from about 1000 mbar to about 3000 mbar.

19. The method of any of claims 1-18, wherein said virus filter is autoclavable.

20. The method of any of claims 1-19, wherein the cell culture medium comprises soy hydrolysate.

21. Use of a virus filter having an effective pore size of maximum 75 nm in a filtration for at least 24 hours for the removal of viral contaminant from a preparation, said preparation being a cell culture medium or at least one component of a cell culture medium, wherein the filtration operates at a volumetric capacity of at least about 2000 L/m².

22. The use of claim 21, wherein the filtration operates at a volumetric capacity of at least about 3000 L/m².

23. The use of claim 22, wherein the filtration operates at a volumetric capacity of at least about 5000 L/m².

24. The use of any one of claims 21-23, wherein filtration is performed for at least about 48 hours up to about 7 months.

25. The use of claim 24, wherein said preparation is subjected to filtration for at least about 72 hours up to about 3 months.

26. The use of any one of claims 21-25, wherein the filtration is a continuous filtration.

27. The use of any one of claims 21-26, wherein filtration is performed at a temperature range from about 2 °C to about 60 °C.

28. The use of claim 27, wherein the filtration is performed at a temperature from about 10 °C to about 40 °C.

29. The use of claim 28, wherein the filtration is performed at a temperature from about 15 °C to about 37°C.

30. The use of any one of claims 21-29, wherein said virus filter achieves at least a 1 Log₁₀ reduction value (LRV) for a viral contaminant.
31. The use of claim 30, wherein said virus filter achieves at least a 4 LRV for a viral contaminant.
32. The use of claim 31, wherein said virus filter achieves at least a 6 LRV for a viral contaminant.
33. The use of any one of claims 21-30, where filtration is performed using two or more filters arranged in series, in parallel or a mixture of both.
34. The use of claim 33, wherein filtration is performed using two filters arranged in parallel in a system of tubes comprising a Y-shaped junction and wherein each filter is in fluid communication with a branch of the Y-shaped junction and a preparation supply source.
35. The use of any one of claims 21-34, wherein filtration is performed at a pressure ranging from about 100 mbar to about 4000 mbar.
36. The use of claim 35, wherein the filtration is performed at a pressure ranging from about 100 mbar to about 3500 mbar.
37. The use of claim 36, wherein the filtration is performed at a pressure ranging from about 1000 mbar to about 3000 mbar.
38. The use of any one of claims 21-37, wherein said virus filter is autoclavable.
39. The use of any one of claims 21-38, wherein the cell culture medium comprises soy hydrolysate.

CLAIMS

1. A method for removing a viral contaminant from a preparation, being a cell culture medium or at least a component of a cell culture medium, comprising the step of:
 - a) Subjecting said preparation to filtration for at least about 24 hours through a virus filter having an effective pore size of maximum 75 nm.
2. The method of claim 1, wherein the filtration operates at a volumetric capacity of at least about 2000 L/m², preferably at least about 3000 L/m², most preferably at least about 5000 L/m².
3. The method of any of claims 1-2, wherein said preparation is subjected to filtration for at least about 48 hours up to about 7 months and preferably about 72 hours up to about 3 months.
4. The method of any of claims 1-3, further comprising the step:
 - b) Feeding the filtrate to a cell culture or to other components also being components of a cell culture medium.
5. The method of any of claims 1-4, wherein the filtration is a continuous filtration.
6. The method of any of claims 1-5, wherein filtration is performed at a temperature from about 2 °C to about 60 °C, preferably about 10 °C to about 40 °C, most preferably about 15 °C to about 37°C.

7. The method of any of claims 1-6, wherein said virus filter achieves at least a 1 Log_{10} reduction value (LRV) for a viral contaminant, preferably at least a 4 Log_{10} reduction value (LRV) for a viral contaminant and most preferably at least 6 Log_{10} reduction value (LRV) for a viral contaminant.
8. The method of any of claims 1-7 where filtration is performed using two or more filters arranged in series, in parallel or a mixture of both.
9. The method of claim 8, wherein filtration is performed using two filters arranged in parallel in a system of tubes comprising a Y-shaped junction and wherein each filter is in fluid communication with a branch of the Y-shaped junction and a preparation supply source.
10. The method of any of claims 1-9, wherein filtration is performed at a pressure ranging from about 100 mbar to about 4000 mbar, preferably from about 100 mbar to about 3500 mbar, most preferably from about 1000 mbar to about 3000 mbar.
11. The method of any of claims 1-10, wherein said virus filter is autoclavable.
12. The method of any of claims 1-11, wherein the cell culture medium comprises soy hydrolysate.
13. Use of a virus filter having an effective pore size of maximum 75 nm in a filtration for at least 24 hours for the removal of viral contaminant from a preparation, being a cell culture medium or at least a component of a cell culture medium.

14. The use of claim 13, wherein the filtration operates at a volumetric capacity of at least 2000 L/m^2 , preferably at least 3000 L/m^2 , most preferably at least 5000 L/m^2 .
15. The use of any of claims 13-14, wherein filtration is performed for at least about 48 hours up to about 7 months and preferably about 72 hours up to about 3 months.
16. The use of any of claims 13-15, wherein the filtration is a continuous filtration.
17. The use of any of claims 13-16, wherein filtration is performed at a temperature range from about 2°C to about 60°C , preferably about 10°C to about 40°C , most preferably about 15°C to about 37°C .
18. The use of any of claims 13-17, wherein said virus filter achieves at least a 1 Log_{10} reduction value (LRV) for a viral contaminant; preferably at least a 4 Log_{10} reduction value (LRV) for a viral contaminant and most preferably at least 6 Log_{10} reduction value (LRV) for a viral contaminant.
19. The use of any of claims 13-18, where filtration is performed using two or more filters arranged in series, in parallel or a mixture of both.
20. The use of claim 19, wherein filtration is performed using two filters arranged in parallel in a system of tubes comprising a Y-shaped junction and wherein each filter is in fluid communication with a branch of the Y-shaped junction and a preparation supply source.
21. The use of any of claims 13-20, wherein filtration is performed at a pressure ranging from about 100 mbar to about 4000 mbar, preferably from about 100

mbar to about 3500 mbar, most preferably from about 1000 mbar to about 3000 mbar.

22. The use of any of claims 13-21, wherein said virus filter is autoclavable.

23. The use of any of claims 13-22, wherein the cell culture medium comprises soy hydrolysate.

24. Use of a preparation, being a cell culture medium or at least a component of a cell culture medium obtainable according to any of claims 1 to 12 for cell culture; pharmaceutical, diagnostic and/or cosmetic preparations as well as in food preparations.