A NOVEL CONTINUOUS FLOW REACTOR FOR LOW PH VIRAL INACTIVATION

FIELD OF THE INVENTION

[0001] The present disclosure generally relates to an apparatus and a process for a novel reactor. More particularly, the present disclosure relates to an apparatus and a process for continuous flow reactor for low pH viral inactivation.

BACKGROUND OF THE INVENTION

[0002] The invention lies on the field of production of biological products like proteins which usually takes place in a bioreactor (fermenter) where e.g. eukaryotic cells are cultivated to produce a protein of interest. Different technologies are established therefore, e.g. fed-batch or continuous or perfusion fermentation. Before use the product needs to be purified. Among the purification steps inactivation of viruses is mandatory, especially when the product is intended for use in humans.

[0003] Presently, virus inactivation at a low pH is performed in a batch reactor. The material to be inactivated (*i.e.*, a liquid which potentially contains the active viruses) is introduced into a batch reactor. The material to be inactivated is brought to a pH of ≤4 by an acidic solution and allowed to stand for the required time. The inactivation of the viruses is effected by contact of the viruses with the acidic solution for a particular product- and process-dependent time. The entire content of the batch reactor experiences inactivation with a virtually identical residence time. Additionally, the virus reduction achieved in each batch is virtually identical.

SUMMARY

[0004] In the disclosure, a viral inactivation device is provided. The viral inactivation device includes at least one continuous viral inactivation reactor including an inlet, an outlet, and a

tubular flow path comprising a set of alternating turns that form a serpentine pattern between the inlet and the outlet. In an aspect, the present disclosure provides a viral inactivation device comprising: at least one continuous viral inactivation reactor including an inlet, an outlet, and a tubular flow path comprising a set of alternating turns that form a serpentine pattern between the inlet and the outlet.

[0005] In an example, the at least one continuous viral inactivation reactor is an in-line tubular continuous viral inactivation reactor.

[0006] In another example, the set of alternating turns comprises at least two alternating turns having an angle of from about 270° to about 280°.

[0007] In a further example, the set of alternating turns comprises from about 2 to about 325 or more alternating turns having an angle of from about 270° to about 280°.

[0008] In yet another example, the tubular flow path includes a diameter of from about 0.6 cm to about 0.7 cm.

[0009] In an example, the set of alternating turns are segmented vertically into at least two stacked layers.

[0010] In a further example, each of the at least two stacked layers comprises 12.5 alternating turns in a single plane, wherein each of the alternating turns includes an angle of from about 270° to about 280°.

[0011] In an example, each of the at least two stacked layers include a thickness of from about 0.7 cm to about 1.2 cm.

[0012] In an example, each of the at least two stacked layers is connected to one another via a 180° turn of the tubular flow path.

[0013] In another example, the at least two stacked layers are 26 layers connected to one another via 25 180° turns of the tubular flow path.

[0014] In a further example, the at least one continuous viral inactivation reactor comprises from about 2 to about 6 viral inactivation reactors connected in series.

[0015] In yet another example, the set of alternating turns generate a vortex to induce mixing a product stream having a laminar flow with a Reynolds Number of from about 187.7 to about 375.5.

[0016] In an example, the tubular flow path includes dimensions such that a product stream is in the continuous viral inactivation reactor for at least 30 minutes.

[0017] In the disclosure, the viral inactivation device includes a low pH continuous viral inactivation reactor having an inlet in fluid communication with a first static mixer and an outlet in fluid communication with a second static mixer; wherein the low pH continuous viral inactivation reactor includes a tube formed of a set of alternating turns. In another aspect, the present disclosure provides a viral inactivation device comprising: a low pH continuous viral inactivation reactor having an inlet in fluid communication with a first static mixer and an outlet in fluid communication with a second static mixer; wherein the low pH continuous viral inactivation reactor includes a tube formed of a set of alternating turns.

[0018] In a further example, the tube includes dimensions such that a product stream is in the low pH continuous viral inactivation reactor for at least 30 minutes.

[0019] In yet another example, each turn in the set of alternating turns comprises an angle of from about 270° to about 280°.

[0020] In an example, the set of alternating turns includes a radius of curvature of from about 0.85 cm to about 2 cm.

[0021] In another example, the tube includes 325 alternating turns.

[0022] In a further example, the tube is segmented into 26 vertical layers connected to one another by 25 tubular flow paths, each having a 180° turn.

[0023] In yet another example, the tube comprises at least 12.5 alternating turns in a single plane.

[0024] In an example, the low pH continuous viral inactivation reactor comprises from about 2 to about 6 viral inactivation reactor connected in series.

[0025] In another aspect, a process for a continuous low pH viral inactivation of a product

stream is provided comprising introducing the product stream to a first static mixer to lower its pH to a predetermined viral inactivation pH; introducing the product stream to be inactivated exiting the first static mixer into an inlet of a tube having a set of turns in a single plane; flowing the product stream through the tube under virus-inactivating conditions; and exiting the product stream from the tube through an outlet of the tube; wherein to lower the pH of the product stream, a low pH buffer is introduced to a first static mixer.

[0026] In a further example, the turns in a single plane form a serpentine pattern.

[0027] In an example, the product stream is introduced to a first static mixer from a protein A capture.

[0028] Additional features and advantages of various examples will be set forth, in part, in the description that follows, and will, in part, be apparent from the description, or may be learned by the practice of various examples. The objectives and other advantages of various examples will be realized and attained by means of the elements and combinations particularly pointed out in the description herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0029] The present disclosure in its several aspects and embodiments can be more fully understood from the detailed description and the accompanying drawings, wherein:

[0030] Fig. 1; illustrates an overall continuous low pH viral inactivation scheme, according to an example of the present disclosure;

[0031] Fig. 2A is a top view of a tubular flow path of a continuous tubular reactor, according to an example of the present disclosure;

[0032] Fig. 2B is a partial perspective view of a continuous tubular reactor, according to an example of the present disclosure;

CLAIMS

We claim:

1. A viral inactivation device comprising:

at least one continuous viral inactivation reactor including an inlet, an outlet, and a tubular flow path comprising a set of alternating turns that form a serpentine pattern between the inlet and the outlet.

2. The device of claim 1, wherein the at least one continuous viral inactivation reactor is an in-line tubular continuous viral inactivation reactor.

3. The device of claim 1 and/or 2, wherein the set of alternating turns comprises at least two alternating turns having an angle of from 270° to 280°.

4. The device of one or more of claims 1 to 3, wherein the set of alternating turns comprises from 2 to 325 or more alternating turns having an angle of from 270° to 280°.

5. The device of one or more of claims 1 to 4, wherein the tubular flow path includes a diameter of from 0.6 cm to 0.7 cm.

6. The device of one or more of claims 1 to 5, wherein the set of alternating turns are segmented vertically into at least two stacked layers.

7. The device of claim 6, wherein each of the at least two stacked layers comprises

12.5 alternating turns in a single plane, wherein each of the alternating turns includes an angle of from 270° to 280° and/or

wherein each of the at least two stacked layers include a thickness of from 0.7 cm to 1.2 cm and/or

wherein each of the at least two stacked layers is connected to one another via a 180° turn of the tubular flow path.

8. The device of claim 7, wherein the at least two stacked layers are 26 layers connected to one another via 25 180° turns of the tubular flow path.

9. The device of one or more of claims 1 to 8, wherein the at least one continuous viral inactivation reactor comprises from 2 to 6 viral inactivation reactors connected in series.

10. The device of one or more of claims 1 to 9, wherein the set of alternating turns is arranged to generate a vortex to induce mixing a product stream having a laminar flow with a Reynolds Number of from 187.7 to 375.5.

11. The device of one or more of claims 1 to 10, wherein the tubular flow path includes dimensions such that a product stream is in the continuous viral inactivation reactor for at least 30 minutes.

12. A viral inactivation device comprising:

a low pH continuous viral inactivation reactor having an inlet in fluid communication with a first static mixer and an outlet in fluid communication with a second static mixer;

wherein the low pH continuous viral inactivation reactor includes a tube formed of a set of alternating turns.

13. The device of claim 12, wherein the tube includes dimensions such that a product stream is in the low pH continuous viral inactivation reactor for at least 30 minutes and/or

wherein each turn in the set of alternating turns comprises an angle of from 270° to 280° and/or

wherein the set of alternating turns includes a radius of curvature of from 0.85 cm to 2 cm and/or

wherein the tube includes 325 alternating turns and/or

wherein the tube is segmented into 26 vertical layers connected to one another by 25 tubular flow paths, each having a 180° turn and/or

wherein the tube comprises at least 12.5 alternating turns in a single plane and/or

wherein the low pH continuous viral inactivation reactor comprises from 2 to 6 viral inactivation reactor connected in series.

14. A process for a continuous low pH viral inactivation of a product stream comprising:

introducing the product stream to a first static mixer to lower its pH to a predetermined viral inactivation pH;

introducing the product stream to be inactivated exiting the first static mixer into an inlet of a tube having a set of turns in a single plane;

flowing the product stream through the tube under virus-inactivating conditions; and

exiting the product stream from the tube through an outlet of the tube;

wherein to lower the pH of the product stream, a low pH buffer is introduced to a first static mixer.

15. The process of claim 14, wherein the turns in a single plane form a serpentine pattern and/or

wherein the product stream is introduced to a first static mixer from a protein A capture.