

Claims

- [Claim 1] A method for preparing a composition comprising ~~highly concentrated~~ antibodies having a high concentration of above 200 g/L by ultrafiltration, wherein the method comprises the steps of:
- 1) regulating the feed flow rate to allow the value of feed pressure applied to an ultrafiltration membrane to increase to 85-100% of a specified maximum feed pressure of an ultrafiltration membrane, wherein the feed flow rate is maintained at 200 LMH (L/m²/hour) or higher; and
 - 2) decreasing the feed flow rate to maintain or decrease the value of the feed pressure applied to the ultrafiltration membrane after the step (1).
- [Claim 2] The method of claim 1, wherein the antibody preparation is processed at ambient temperature.
- [Claim 3] The method of claim 1, wherein the antibody preparation is processed at a temperature from 10 to 30 degrees C.
- [Claim 4] The method of claim 1, wherein the antibody preparation is processed at a temperature from 15 to 30 degrees C.
- ~~[Claim 5] The method of claim 1, wherein the highly concentrated antibodies have a high concentration of above 100 g/L or a viscosity above 2 mPa.s.~~
- ~~[Claim 6] The method of claim 1, wherein the highly concentrated antibodies have a high concentration of above 200 g/L or a viscosity above 10 mPa.s.~~
- [Claim ~~7~~5] The method of claim 1, wherein the highly concentrated antibodies have a high concentration of above 250 g/L or a viscosity above 40 mPa.s.
- ~~[Claim 8] The method of claim 1, wherein the feed flow rate in step (1) is maintained at 200 LMH (L/m²/hour) or higher.~~
- [Claim ~~9~~6] The method of claim 1, wherein the feed flow rate in step (1) is maintained at 250 LMH (L/m²/hour) or higher.
- [Claim ~~10~~7] The method of claim 1, ~~8 and 9~~ or 6, wherein the feed flow rate in step (1) is maintained at a constant rate.
- [Claim ~~11~~8] The method of claim 1, wherein the maximum value of the feed pressure applied to an ultrafiltration membrane in step (1) is from 2.0 bar to 4.0 bar.
- [Claim ~~12~~9] The method of claim 1, wherein the maximum value of the feed pressure applied to an ultrafiltration membrane in step (1) is 3.5 bar.
- ~~[Claim 13] The method of claim 1, wherein the maximum value of the feed pressure applied to an ultrafiltration membrane in step (1) is 85-100% of the specified maximum feed pressure of the ultrafiltration~~

membrane.

- [Claim ~~14~~10] The method of claim 1, wherein step (1) is transitioned to step (2) when the retentate solution is concentrated to a protein concentration greater than 200 g/L.
- [Claim ~~15~~11] The method of claim 1, wherein step (1) is transitioned to step (2) when the retentate solution is concentrated to a protein concentration equal or greater than 220 g/L.
- [Claim ~~16~~12] The method of claim 1, wherein step (1) is transitioned to step (2) when the retentate solution is concentrated to a protein concentration equal to 240 g/L.
- [Claim ~~17~~13] The method of claim ~~13~~1, wherein the feed flow rate after the value of the feed pressure is decreased in step (2) is maintained at a constant rate.
- [Claim ~~18~~14] The method of claim ~~13~~1 or ~~17~~13, wherein the feed flow rate after the value of the feed pressure is decreased in step (2) is maintained at 120 LMH (L/m²/hour) or lower.
- [Claim ~~19~~15] The method of claim ~~13~~1 or ~~17~~13, wherein the feed flow rate after the value of the feed pressure is decreased in step (2) is maintained at 80 LMH (L/m²/hour) or lower.
- [Claim ~~20~~16] The method of claim 1, wherein the value of the feed pressure applied to an ultrafiltration membrane in step (2) is maintained at a constant value.
- [Claim ~~21~~17] The method of claim 1, wherein the value of the feed pressure applied to an ultrafiltration membrane in step (2) is maintained within 85-100% of the specified maximum feed pressure of the ultrafiltration membrane by reducing the feed flow rate.
- [Claim ~~22~~18] The method of claim ~~20~~16 or ~~21~~17, wherein the feed flow rate is automatically regulated in a manner to maintain the feed pressure within 85-100% of the specified maximum feed pressure of the ultrafiltration membrane by a feedback control between a feed pressure and a feed flow rate.
- [Claim ~~23~~19] The method of claim 1, further comprising between step (1) and step (2), the following step of:
3) recirculating the antibody preparation through the membrane with a permeate valve closed.
- [Claim ~~24~~20] The method of claim ~~23~~19, wherein the antibody preparation is recirculated with a retentate pressure control valve fully open.
- [Claim ~~25~~21] The method of claim ~~23~~19, wherein the feed flow rate in step (3) is

maintained at a constant flow rate between 5 to 120 LMH (L/m²/hour).

- [Claim ~~26~~22] The method of claim ~~23~~19, wherein the feed flow rate in step (3) is maintained at a constant flow rate between 10 to 80 LMH (L/m²/hour).
- [Claim ~~27~~23] The method of claim 1, wherein the buffer composition of the antibody preparation is between 10 to 30 mmol/L histidine.
- [Claim ~~28~~24] The method of claim 1, wherein the buffer composition of the antibody preparation is 20 mmol/L histidine.
- [Claim ~~29~~25] The method of claim 1, wherein the pH of the antibody preparation is between pH 3.0 and pH 10.0.
- [Claim ~~30~~26] The method of claim 1, wherein the pH of the antibody preparation is between pH 5.5 and pH 6.5.
- [Claim ~~31~~27] The method of claim 1, wherein the pH of the antibody preparation is pH 6.0.
- [Claim ~~32~~28] The method of claim 1, wherein the ultrafiltration membrane has a molecular weight cut off of 50 kDa or less.
- [Claim ~~33~~29] The method of claim 1, wherein the ultrafiltration membrane has a molecular weight cut off of 30 kDa or less.
- [Claim ~~34~~30] The method of claim 1, wherein the composition comprises ~~highly concentrated~~ anti-human interleukin-6 receptor monoclonal antibodies having a high concentration of above 200 g/L.
- [Claim ~~35~~31] The method of claim ~~34~~30, wherein the composition comprises ~~highly concentrated~~ tocilizumab having a high concentration of above 200 g/L.
- [Claim ~~36~~32] A liquid composition which comprises ~~highly concentrated antibodies~~ the composition prepared by the method of claim 1.
- [Claim ~~37~~33] A pharmaceutical liquid composition which comprises ~~highly concentrated antibodies~~ the composition prepared by the method of claim 1 and a pharmaceutically acceptable carrier.
- [Claim ~~38~~34] A method for preparing a composition comprising ~~highly concentrated~~ proteins having a high concentration of above 200 g/L by ultrafiltration, wherein the method comprises the steps of:
 1) regulating the feed flow rate to allow the value of feed pressure applied to an ultrafiltration membrane to increase to 85-100% of a specified maximum feed pressure of an ultrafiltration membrane, wherein the feed flow rate is maintained at 200 LMH (L/m²/hour) or higher; and
 2) decreasing the feed flow rate to maintain or decrease the value of the feed pressure applied to the ultrafiltration membrane after the step (1).