CLAIMS

1. A method for dynamic filtration of a cross-linked biopolymer-based hydrogel comprising the following steps:

(a) transferring a cross-linked biopolymer-based hydrogel in a dynamic filtration device which is equipped with semipermeable filter disc(s) and diafiltrating the gel comprising the steps of:

(i) concentrating the gel by applying a rotational speed within the range of 20 1/min to 500 1/min and a overpressure within the range of 0.5 to 6 bar to a predetermined concentration; or pumping the gel directly into the process chamber of the dynamic filtration device;

(ii) conducting a diafiltration to reduce unwanted molecules by applying a rotational speed within the range of 20 1/min to 500 1/min and a overpressure within the range of 0.5 to 6 bar;

(b) optionally adding a mixture comprising a non-cross-linked polymer, in particular non cross-linked hyaluronic acid, and water to the gel.

2. A method according to Claim 1, in which the biopolymer-based hydrogel is made of a polymer which is selected from the group consisting of hyaluronic acid, heparosan, alginate, pectin, gellan gum, chondroitin sulfate, keratan, keratan sulfate, heparin, heparin sulfate, cellulose, chitosan, carrageenan, xanthan, or salts or derivatives thereof or combinations thereof.

3. A method according to Claim 1 or 2, in which the hydrogel is cross-linked by means of a chemical cross-linking agent, and the hydrogel contains a surplus of the chemical cross-linking agent, in which surplus of the chemical cross-linking agent and / or other unwanted molecules are removed.

4. A method according to Claim 1, 2 or 3, in which the semipermeable filter disc(s) exhibit a pore size of 5 nm to 2µm, more particularly a pore size of 30 nm to 600 nm, more particularly a pore size of 80 nm to 300 nm, particularly a pore size of 5 nm to 60 nm.

5. A method according any preceding claim, in which the dynamic filtration device is equipped with 1 to 10 semipermeable filter disc(s).

6. A method according any preceding claim, in which the semipermeable filter disc(s) are made of ceramic, metal or polymer material.

7. A method according any preceding claim, in which the hydrogel is cross-linked by means of BDDE, and the hydrogel contains a surplus of BDDE, in which surplus of BDDE and / or other unwanted molecules are removed.

8. A method according any preceding claim, in which the biopolymer-based hydrogel is made of hyaluronic acid, the diafiltration in step (ii) is performed by applying a rotational speed within the range of 20 1/min to 500 1/min and a pressure within the range of 0.5 to 3 bar, and the diafiltration in step (ii) is conducted at a concentration of the hydrogel in the range of 10 to 70 mg/g.

9. A method according any preceding claim, in which during or after diafiltration an anesthetic agent is added to the gel.

10. A method according to Claim 9, in which during or after diafiltration lidocaine is added to the gel.

11. A method according any preceding claim, in which the diafiltration in step (ii) and optionally the concentration step (i) are performed at a temperature in the range of from 60 °C to 70 °C and for a time period of from 2 to 4 hours.

12. A method according any preceding claim, in which the gel is sterilized in the device at 121 °C to 135°C with a holding time of about 2 to 30 minutes.

13. A method according any preceding claim, in which the method is conducted in less than 10 hours, in particular in less than 5 hours.

14. A cross-linked biopolymer-based hydrogel obtainable by a method according to any preceding claim.

15. Non-surgical use of a hydrogel according to Claim 14 for aesthetic applications, in particular soft tissue augmentation.

CLAIMS

1. A method for dynamic filtration of a cross-linked biopolymer-based hydrogel comprising the following steps:

(a) transferring a cross-linked biopolymer-based hydrogel in a dynamic filtration device which is equipped with 1 to 10 semipermeable filter disc(s) and diafiltrating the cross-linked biopolymer-based hydrogel comprising the steps of:

(i) concentrating the cross-linked biopolymer-based hydrogel by applying a rotational speed within the range of 20 1/min to 500 1/min and a overpressure within the range of 0.5 to 6 bar to a predetermined concentration; or pumping the cross-linked biopolymer-based hydrogel directly into the process chamber of the dynamic filtration device;

(ii) conducting a diafiltration at a concentration of the cross-linked biopolymer-based hydrogel in the range of from 10 to 70 mg/g using a buffer solution to reduce unwanted molecules by applying a rotational speed within the range of 20 1/min to 500 1/min and a overpressure within the range of 0.5 to 6 bar;

(b) optionally adding a mixture comprising a non-cross-linked polymer, in particular non cross-linked hyaluronic acid, and water to the cross-linked biopolymer-based hydrogel.

2. A method according to Claim 1, in which the biopolymer-based hydrogel is made of a polymer which is selected from the group consisting of hyaluronic acid, heparosan, alginate, pectin, gellan gum, chondroitin sulfate, keratan, keratan sulfate, heparin, heparin sulfate, cellulose, chitosan, carrageenan, xanthan, or salts or derivatives thereof or combinations thereof.

3. A method according to Claim 1 or 2, in which the hydrogel is cross-linked by means of a chemical cross-linking agent, and the hydrogel contains a surplus of the chemical cross-linking agent, in which surplus of the chemical cross-linking agent and / or other unwanted molecules are removed.

4. A method according to Claim 1, 2 or 3, in which the semipermeable filter disc(s) exhibit a pore size of 5 nm to 2µm, more particularly a pore size of 30 nm to 600 nm, more particularly a pore size of 80 nm to 300 nm, particularly a pore size of 5 nm to 60 nm.

5. A method according any preceding claim, in which the semipermeable filter disc(s) are made of ceramic, metal or polymer material.

6. A method according any preceding claim, in which the hydrogel is cross-linked by means of BDDE, and the hydrogel contains a surplus of BDDE, in which surplus of BDDE and / or other unwanted molecules are removed.

7. A method according any preceding claim, in which the biopolymer-based hydrogel is made of hyaluronic acid, the diafiltration in step (ii) is performed by applying a rotational speed within the range of 20 1/min to 500 1/min and a pressure within the range of 0.5 to 3 bar.

8. A method according any preceding claim, in which during or after diafiltration an anesthetic agent is added to the cross-linked biopolymer-based hydrogel.

9. A method according to Claim 8, in which during or after diafiltration lidocaine is added to the cross-linked biopolymer-based hydrogel.

10. A method according any preceding claim, in which the diafiltration in step (ii) and optionally the concentration step (i) are performed at a temperature in the range of from 60 °C to 70 °C and for a time period of from 2 to 4 hours.

11. A method according any preceding claim, in which the cross-linked biopolymer-based hydrogel is sterilized in the device at 121 °C to 135°C with a holding time of 2 to 30 minutes.

12. A method according any preceding claim, in which the method is conducted in less than 10 hours, in particular in less than 5 hours.