chromatography and crystallization, and wherein monomeric impurities are removed.

Summary

A process has been sought wherein the crude dimeric contrast agent is purified providing a high yield, wherein crystallisation of crystals is avoided, which is easy to scale up and which provides a purified agent in short time. A process has now been identified using membrane technology to remove monomeric compound impurities and salts from the crude product of dimeric X-ray contrast agents.

Accordingly, the disclosure provides a process for the purification of a crude dimeric X-ray contrast agent product comprising the step of

i) passing a solution of the crude product across a membrane (M1) such that monomeric compound impurities and salts cross the membrane (permeate, P1) and the dimeric X-ray contrast agent passes over the membrane (retentate, R1)

providing a purified dimeric X-ray contrast agent.

In a first aspect, there is provided a process for the purification of a crude dimeric X-ray contrast agent product comprising the steps of

i) passing a solution of the crude product across a membrane M1 having a cut-off size between 950 and 1200 Da, such that monomeric compound impurities having a molecular weight of less than 900 Da and salts cross the membrane to form a permeate P1 and the dimeric X-ray contrast agent passes over the membrane to form a retentate R1,

providing a purified dimeric X-ray contrast agent.

Brief Description of the drawings

Figure 1 shows the process of the first aspect wherein a crude product is purified by separating purified product from monomeric impurities and salts.

Claims

1. A process for the purification of a crude dimeric X-ray contrast agent product comprising the steps of

   i) passing a solution of the crude product across a membrane M1 having a cut-off size between 950 and 1200 Da, such that monomeric compound impurities having a molecular weight of less than 900 Da and salts cross the membrane to form a permeate P1 and the dimeric X-ray contrast agent passes over the membrane to form a retentate R1,

providing a purified dimeric X-ray contrast agent.

2. A process as claimed in claim 1 wherein the dimeric X-ray contrast agent has a molecular weight of 1400-1700 Da.

3. A process as claimed in claim 1 wherein the dimeric X-ray contrast agent is loforminol or Iodixanol.

4. A process as claimed in any of the claims 1 to 3 wherein the retentate R1 of the step (i) is retained and collected.

5. A process as claimed in any of the claims 1 to 4 wherein the purified dimeric X-ray contrast agent obtained holds a purity of at least 98 %.

6. A process as claimed in any of the claims 1 to 5 comprising a second step

   ii) wherein the permeate from step i) P1 is passed across another membrane M2 such that salts cross this membrane to form a permeate P2 and the monomeric compound impurities passes over the membrane to form a retentate R2, and wherein the retentate R2 is retained.

7. A process as claimed in any of the claims 1 to 6 wherein the permeate P1 from step i), or the retentate R2 from step (ii), is subject to another round of purification by repeating step (i) of the process to recover dimeric X-ray contrast agent lost in the first round.

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8. A process as claimed in claim 6 wherein the retentate R2 is transferred to the crude product and mixed with this, or is combined with a feed stream from the crude product, before repeating step i).