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Separation and Purification Technology 22-23 (2001) 79–87

Separation
Purification
Technology

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Design of sanitary and sterile UF- and diafiltration plants

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Abstract

The new plate and frame module M39 from DSS is introduced. The main advantage is a reduction of pressure difference over the module compared to previous modules. This enables adjustment of the permeate flux according to needs. Sterile and sanitary design is discussed and the DSS UF-spiral constructed for heat sterilisation is introduced. The advantages and disadvantages of batch and continuous ultrafiltration plants are discussed. A new diafiltration concept — counter current diafiltration — is introduced and discussed together with the possibility of using purified permeate as diafiltration water. Ultrafiltration is only one part of a total factory. An important factor in obtaining the best economic and environmental process is determining the optimum overall process layout. The new diafiltration concept offers advantages by reducing environmental problems and investment requirements.

Keywords: Sterile and sanitary design; Counter current diafiltration; Ultrafiltration

1. The DSS modules

The food, biotech and pharmaceutical industries invariably require UF-plants with a good sanitary design, and some applications require heat sterilisation of the equipment at 121°C.

The plate and frame modules M38 and the new type M39 produced by DDS are ideal for sanitary UF plants. The main construction material is polysulphone.

M38 is normally used with three to five sections, operating with a typical inlet pressure of 4 bar and an outlet pressure of 1–2 bar. It was evident that many applications would benefit considerably if the operating pressure was constant across the entire module. The result is the M39 module with following main features (Fig. 1):

- a large area of the inlet and outlet ports to enable treatment of a large flow of liquid in a single-pass module with only one section;
- channels of the same width, providing for excellent liquid distribution;
- two different channel heights, ≈ 0.5 and 1.4 mm, for both low- and high-viscosity applications.

The use of a single section with consequent lower pressure difference offers two advantages (see Fig. 2):

1. Constant pressure means that permeate production is kept more constant during the manufacturing process.
2. Permeate production can be controlled by

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PII: S1383-5866(00)00144-1

changing the pressure. This is not practically possible in a plant with multi-section modules because most of the membrane always has a pressure giving the maximum flux. This is important if production has to be constant and adjusted to another unit operation.

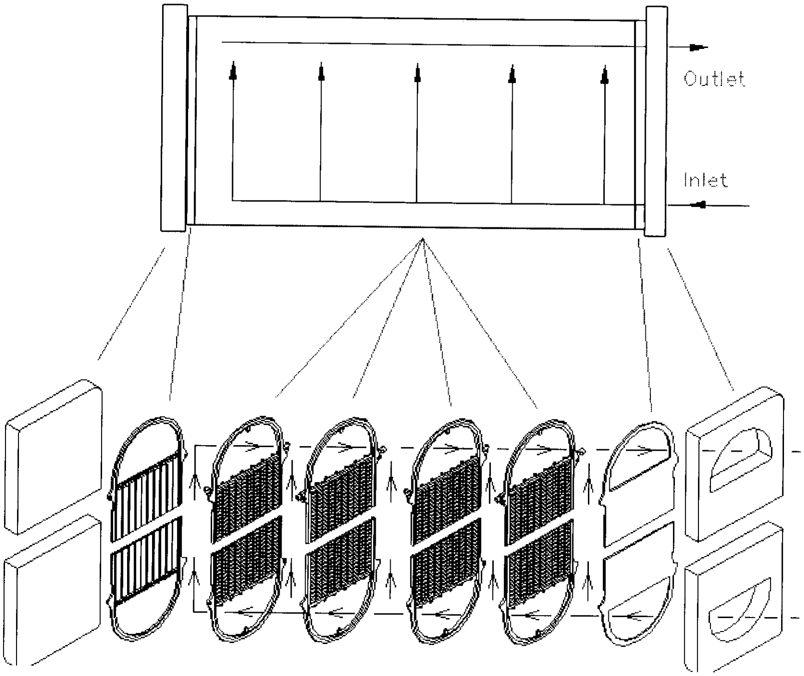

Fig. 1. Drawing showing the principle of DSS Module 39. The module normally has only one section. The large manifold channels for feed inlet and concentrate outlet allow the construction of modules with a membrane area up to 90 m^2. The feed flows between membranes supported by the spacers. All flow channels have the same geometry, giving identical flow conditions in all channels.

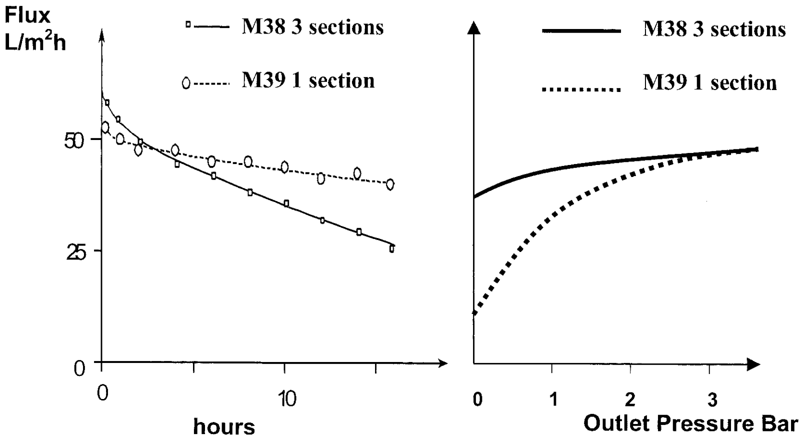

Fig. 2. The diagram on the left shows the relation between hours of operation and instant flux at constant pressure. The diagram on the right shows the relationship between pressure and instant flux. Curves are shown both for the DSS M38 with three sections, and for the DSS M39 with one section. It is possible to adjust the flux of the M39 within wide limits, whereas the M38 has a high minimum flux.

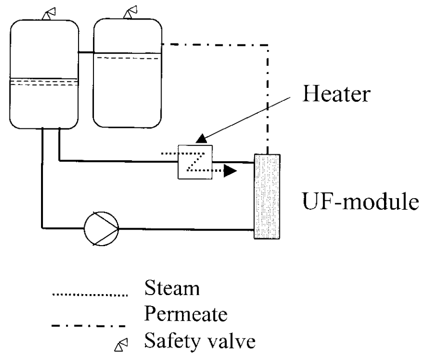

Fig. 3. Method of heat sterilisation for DSS spirals. The temperature of the entire system is increased to 121°C using the heater. The UF-spiral is placed under the tanks. This prevents bubble formation on both the concentrate and permeate side.

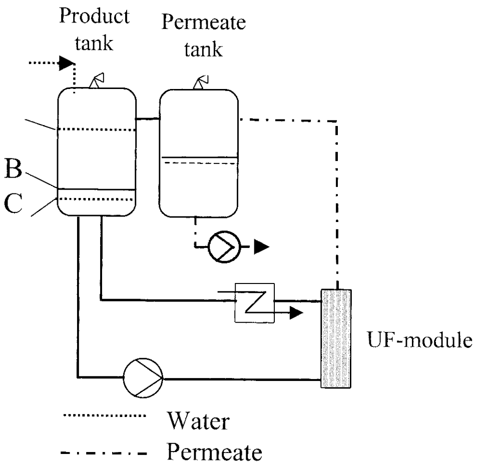

Fig. 4. Principle of batch ultrafiltration with diafiltration. A batch is started at level A. When the level has reached B, water addition to the product tank is started and the level is kept constant until the composition is correct. Ultrafiltration without water addition continues until level C is reached. This is the final concentration.

2. Heat sterilisation of UF-spirals

The spiral wound UF modules of DDS featuring both the traditional construction with polyester spacers and a construction where the membrane support and all spacers are made from polypropylene. The latter material enables them to be heat sterilised at 121°C.

During heat sterilisation, it is important to prevent cavitation and boiling inside the system. Fig. 3 shows the principles. The pressure in the module is higher than in the tanks, both on the concentrate and the permeate side. The same temperature is secured in both the tanks and the module by heating with a heat exchanger at the module outlet. The temperature must reach 121°C everywhere in the system, requiring effective insulation and temperature control in the permeate system.

3. Sanitary, sterile or both?

Before proceeding, it is necessary to define the concepts of *sanitary design* and *sterile design*.

Sanitary design of a plant means, most importantly, a plant construction that permits satisfactory CIP cleaning in order to prevent the growth of micro-organisms during processing and ensure a microbiologically satisfactory product.

In addition, *sanitary design* means polished surfaces that prevent growth of bacteria on the surfaces, short retention time for all liquid entering the plant, and the absence of dead pockets or air pockets in the system.

Sterile design means that the whole plant (filters, pumps, tanks, pipes, etc.) can be heat sterilised at 121°C, or sterilised in another manner that decreases the bacterial count by the factor 10^{12}. The plant must be constructed in such a manner that eliminates any risk of micro-organism contamination from outside.

In addition, *sterile design* means that the plant is totally closed, stuffing boxes are either steam traced or have bellows, and that the entire plant is normally kept above atmospheric pressure. The retention time for the product is normally not important as no microbiological growth takes place.

A sanitary plant does not need to be sterile. Most sanitary plants are, in fact, not sterile simply because the feed is not sterilised. A sterile plant does not always have a sanitary design, although, in most cases, sterile plants do follow the main rules for sanitary design.

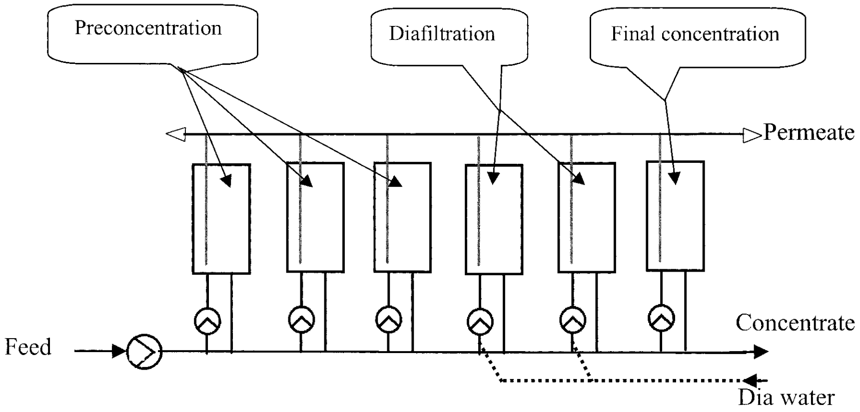

Fig. 5. Principle of a traditional UF-plant with pre-concentration, diafiltration and final concentration. The plant consists of a number of loops in series. Each loop consists of a pump and an UF module. In the first three loops, the liquid is concentrated. In the next two loops diafiltration takes place, i.e. an amount of water is added corresponding to the amount of permeate produced in these modules. In the last module, the product is concentrated to the final concentration. The module types in a continuous plant can be different for different concentration.

The purpose of an UF-plant is usually to divide a solution with solutes with high and low molecular weight into:

1. A concentrate with high concentration of the high molecular weight solute.
2. A permeate with ≈0% of high molecular weight solute, and with as high a concentration as possible of the low molecular weight solutes.

The valuable product can be either the concentrate, the permeate, or both.

4. Batch or continuous system?

The UF-process normally consists of three stages:

1. A pre-concentration where the concentrate volume is reduced by UF. The product is divided into a concentrate with macromolecules, and a permeate without macromolecules. The concentration of solutes with low molecular weight will be almost the same in the concentrate and in the permeate.
2. A diafiltration with simultaneous water addition and UF. This process purifies the concentrate as the small molecules enter the permeate.
3. A final concentration increasing the concentration of macromolecules in the concentrate.

The UF process can either be a batch or continuous process.

In the batch process (Fig. 4) the entire batch is in the tank when the process is started (level A). The batch is ultrafiltered until the level reaches level B. Water is now added and ultrafiltration continues until the product has the required purity. Water addition is then stopped but ultrafiltration continues until level C is reached.

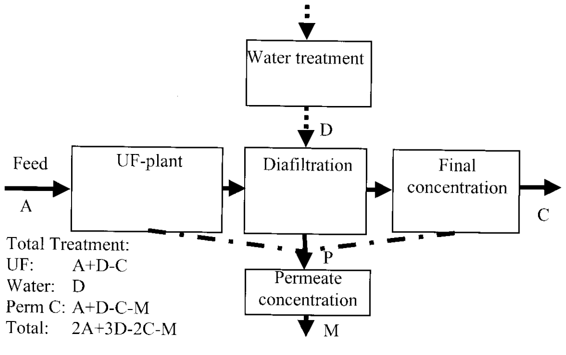

Fig. 6. The total UF-plant. The total plant consists of more than the UF-plant with diafiltration and final concentration. In most cases, a RO plant treats the water and a plant to concentrate the permeate is required. It is important to minimise the investment requirement of the total plant. The investment can be expressed using the sum of the permeates for all the plants involved.

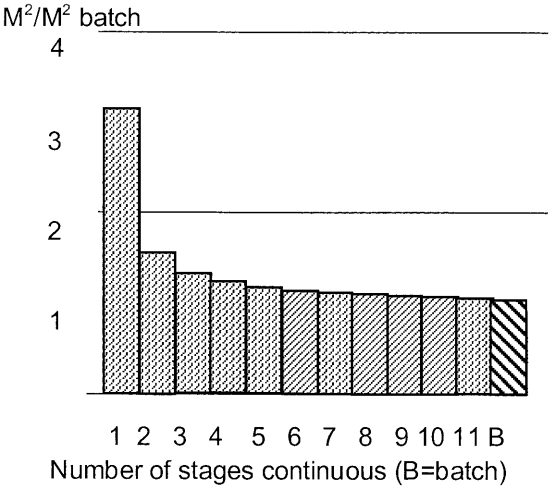

Fig. 7. The ratio between the amount of diafiltration water and feed in traditional continuous diafiltration and in batch diafiltration purifying a protein solution.

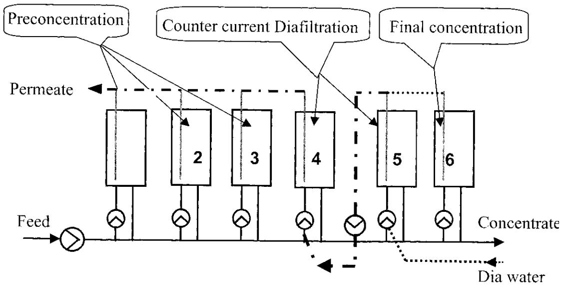

Fig. 8. Principle of counter current diafiltration. Diafiltration water is added to loop 5. The permeate from loop 5 is added to loop 4 instead of diafiltration water.

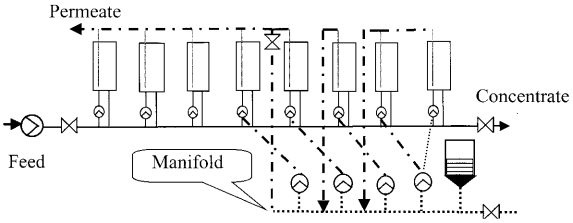

Fig. 9. Principle of counter current diafiltration with diafiltration manifold. Diafiltration water is added to one end of a manifold according to the level of the dia-tank. Permeate from the diafiltration modules returns to the manifold after the supply of diafiltration liquid to the next module.

The continuous process (Fig. 5) consists of a number of recirculation stages in series. The initial stages comprise a concentration process. This is followed by a number of stages in which water is added — the diafiltration stage. The last stage is where final concentration takes place.

A continuous plant has more components than a batch plant, increasing the risk of contamination entering the plant. For example, all pumps normally have washing water on the stuffing boxes. This special water system must be included in both the CIP process and the sterilisation.

5. The total plant

A total process includes other unit operations in addition to the UF plant. Fig. 6 shows processes that are almost always necessary. The water used for diafiltration, and normally also cleaning water and water used for stuffing boxes etc., has to be purified. This will often be achieved using an RO or NF plant. The permeate also has to be concentrated, even if the product in the permeate is not particularly valuable, as environmental considerations preclude disposal via the sewer.

In total, this means that a volume which is twice the flow into the plant, minus the concentrate, plus three times the amount of diafiltration water, minus the permeate concentrate volume, has to be filtered through a membrane or removed in another way.

As it is necessary in reality to install a membrane area that can filter three times the diafiltration water volume, it is important to find ways of decreasing this amount.

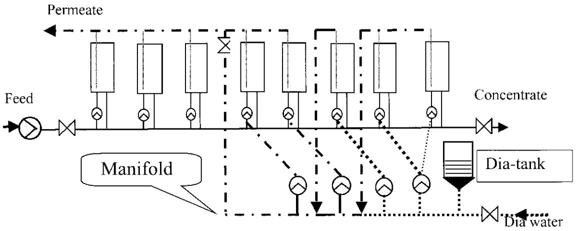

Fig. 10. Principle of counter current diafiltration with bypass of one module. The two last diafiltration modules receive diafiltration water.

Table 1
Size and consumption of diafiltration water for different diafiltration systems

Number of diafiltration stages	M^2 filter/stage diafiltration	M^2 total diafiltration	Dia-liquid each stage (l/h)	Dia-water total (l/h)
Counter current diafiltration				
2	4.10	8.20	87.9	87.9
4	2.06	8.26	44.3	44.3
6	1.67	10.0	35.8	35.8
8	1.51	12.1	32.5	32.5
Counter current diafiltration with one module bypass				
4	1.43	5.72	30.6	61.2
6	1.03	6.21	22.2	44.4
8	0.88	7.04	18.9	37.7
Traditional continuous diafiltration				
2	3.55	7.10	76.1	152.2
4	1.23	4.94	26.5	105.9
6	0.74	4.41	15.7	94.5
8	0.52	4.16	11.1	89.1
Batch diafiltrering				

M^2 diafiltration	Dia-water total (l/h)
3.67	78.8

Table 2
Plant capacity in percent of feed

Unit operation	Traditional continuous diafiltration six stages	Counter current diafiltration with by-pass six stages	Counter current with by-pass and recirculation
UF concentration	71	71	71
Diafiltration	95	133	133
Final concentration	9	9	9
Water treatment	95	44	0
Permeate concentration	165	114	114

5.1. Batch plants have the following advantages

They are easy to sterilise. The whole system of tanks etc. can be heat treated together.

They are easy to control. Concentration is performed until a defined concentration is achieved in the tank. Diafiltration is performed until a defined product purity is achieved. Only automatic pressure control is needed together with level control.

Batches are kept separate. This is often important in the pharmaceutical industry.

Efficient diafiltration. Less diafiltration water is required to remove solutes than in traditional continuous UF-plants.

5.2. The disadvantages of batch plants are

Not continuous production. This is often a disadvantage, especially if the rest of the production is continuous.

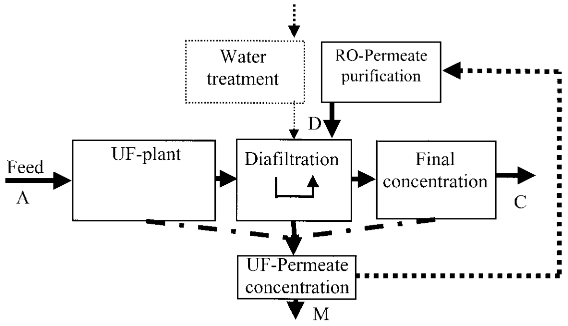

Fig. 11. Diagram of total system with counter current diafiltration and reuse of RO-permeate as diafiltration water. The wastewater production is reduced as shown in Table 3.

The same types of module are used for all concentrations. This is often a serious disadvantage. The modules have to be able to handle the highest viscosity reached. High-viscosity modules are not very efficient at low viscosity, and they have a high energy consumption when recycling liquid over the module.

Batch plants have long retention time. This is probably the most serious disadvantage for sanitary plants operating on non-sterile liquids.

5.3. Continuous plants have the following advantages

Constant production. This is important in a process involving several unit operations in series, especially if short retention time is needed in order to maintain product quality.

Different modules can be used for different viscosities. This saves pumping energy.

Short retention time. This is a must for many applications.

5.4. The disadvantages are

More complicated control. Automatic control is more complicated than in a batch plant because a continuous control of concentrations is needed. This is not really a serious disadvantage, but it increases investment requirements.

Many components are needed. This means a more complicated CIP system, and many places that can cause contamination of the liquid.

Less efficient diafiltration. Batch diafiltration is more efficient than traditional continuous diafiltration. Only with a high number of diafiltration modules in series can almost the same efficiency be achieved.

This is probably one of the most serious disadvantages of traditional continuous plants. As mentioned above, equipment is required to treat three times the amount of diafiltration water.

Fig. 7 shows the consumption of diafiltration water in a continuous plant compared with a batch plant. The number of diafiltration stages has to be quite large in order to achieve an efficiency approaching that of batch diafiltration.

Theory and examples of diafiltration plants are described by Blatt et al. [1], Madsen [2], Hansen [3] and Cheryan [4].

6. Counter current diafiltration

In reality, diafiltration is a cross-flow extraction. Benefits can possibly be achieved by intro-

Table 3
Wastewater production with different diafiltration systems and with permeate recirculation

Method	1. Traditional continuous, six stages	2. Counter current with by-pass, normal diafiltration water six stages	3. As 2, recirculation of permeates
Water purification RO-concentrate	19	9	0
Permeate concentration	165	114	70
Total waste water	184	123	70

ducing some type of counter current extraction in the diafiltration process.

Fig. 8 shows the principle of counter current diafiltration by adding diafiltration water to module 5. The permeate from module 5 is added to module 4 instead of diafiltration water. The concentration difference between the diafiltration liquid and the permeate is lower than in traditional diafiltration, but we use less water and get less permeate.

The process shown in Fig. 8 has a stability problem as independent control of diafiltration liquid in modules 4 and 5 is not possible. A practical trial produced a too high concentration in module 3 as the diafiltration prevented product from proceeding from module 3 to module 4.

This problem is solved as shown in Fig. 9, a plant with four-stage counter current diafiltration in which a manifold is introduced. Water enters at one end, and permeate from the diafiltration modules enters the manifold between the pumps feeding diafiltration liquid to the modules.

This ensures that the modules receive the required liquid, even if the diafiltration modules not have exactly the same capacity.

The required membrane area for counter current diafiltration can be reduced by by-passing one module as shown in Fig. 10.

Table 1 shows an example. The necessary membrane area for diafiltration and amounts of diafiltration water are shown for the purification of a 4% protein solution with 5% low molecular weight solute. The membrane rejection for the low molecular weight solute is 5%. The membrane rejection for protein is 100%. The diafiltration takes place at 14% protein in concentrate with the aim of producing a protein with 98% purity in dry matter. In the final concentration, the protein concentration is increased to 20%. All amounts are expressed as a percentage of the feed.

If six diafiltration stages are used, traditional continuous diafiltration requires use of 95% of the diafiltration water amount. Counter current diafiltration requires only 36% of the diafiltration water amount. This increases to 44% if one module is by-passed during diafiltration. The batch process would require 79% of the diafiltration water amount.

It is seen that counter current diafiltration uses less diafiltration water than the batch process. The membrane area used for diafiltration has to be increased compared with the traditional process with 6 stages, direct counter current requires 10 m^2/100 l/h feed, one-stage by-pass counter current requires 6.2 m^2/100 l/h feed, while the traditional continuous process requires only 4.4 m^2/100 l/h feed.

This increase in membrane area means, however, a reduction in equipment requirements in the total process. Water treatment plant and permeate concentration plant requirements are reduced, resulting in a reduction of the total amount of liquid filtered from 435 to 370 l/h for 100 l/h feed. Table 2 shows the capacity of the different unit operations.

7. Diafiltration water quality

The quality of diafiltration water is an important point. The bacteriological quality has to be satisfactory and the water must have a very low content of both inorganic and organic solutes. Drinking water is normally not sufficient for this purpose, thus necessitating water treatment. This poses the question: Can we produce a satisfactory quality by reverse osmosis of permeate from the ultrafiltration?

Fig. 11 shows the principle. We recycle purified permeate. This has actually been implemented in several applications. The advantage is that no new solutes are introduced into the system and that the amount of wastewater is reduced. Table 3 shows wastewater production for different methods.

If RO is used for water purification, an amount corresponding to at least 20% of the produced water is normally wasted from the RO-plant as concentrate. The permeate, or condensate from a permeate concentration, also comprises wastewater unless it is recycled. In total, we can use the new method to reduce the amount of wastewater to only 40% of that resulting from the traditional process.

The main objection to this process is the risk of bacteriological contamination. However, different steps can eliminate this risk. First of all a short retention time is needed. If the water is stored, this must take place above 80°C or below 4°C. The water system must be included in the CIP system, and the water produced must have low BOD. A low pH is also an advantage.

8. Conclusions

The new diafiltration concept, counter current diafiltration decreases the necessary amount of diafiltration water. As diafiltration water normally has to be treated with RO before use and has to be removed again by evaporation or RO, it is advantageous instead to install the necessary additional membrane area for counter current diafiltration.

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