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Comparison of spiral wound and hollow Fiber microfiltration membranes for milk protein fractionation

Hilda Lucy Nyambura [a,*], Anja E.M. Janssen [a], Remko M. Boom [a], Albert van der Padt [a,b]

[a] Food Process Engineering Group, Wageningen University & Research, P.O. Box 17, 6700AA Wageningen, the Netherlands
[b] FrieslandCampina, Stationsplein 4, 3818 LE, Amersfoort, the Netherlands

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ABSTRACT

Polymeric spiral wound membranes have been commonly used for skim milk fractionation to separate casein and serum proteins. In the recent years the use of hollow fiber membranes has gained interest. This is due to the configurational advantages that they possess such as open flow channels that aid in controlling fouling. The efficiency of hollow fiber and spiral wound membranes during skim milk fractionation at 10 °C was investigated, while operating in batch diafiltration mode using reverse osmosis water. It was observed that permeate flux of hollow fiber membranes was significantly higher than that of the spiral wound membrane. For preconcentration purposes only, both membrane configurations demonstrated similar filtration behavior as filtration is mainly controlled by the accumulated fouling layer of casein micelles on the membrane surface, and not the membrane itself. However, hollow fiber membranes were observed to have higher serum protein concentration in the permeate. During diafiltration, spiral wound membranes retained higher concentration of serum protein as compared to the hollow fiber membranes, resulting in a lower serum protein permeate yield. Hollow fiber membranes achieve higher serum protein purity compared to spiral wound membranes when the serum protein yield of both membranes is kept constant. For combined preconcentration and diafiltration purposes, hollow fiber membranes perform better.

1. Introduction

Membrane fractionation of skim milk into casein and serum protein is an established practice in the dairy industry [6,11,42,44]. Microfiltration membranes, such as tubular ceramic membranes [16,37,40,41] and polymeric flat sheet membranes in spiral wound configuration [11,19,23] have been used for the past decades. Spiral wound membranes have higher packing density and are more cost effective but more complex to clean compared to ceramic membranes. Ceramic membranes are however durable and more resistant to heat and chemicals and have better separation efficiency compared to spiral wound membranes [17,46]. Hollow fiber membranes combine some of the advantages of polymeric spiral wound membranes and ceramic membranes, since they have large membrane area per module, have open channels, are more cost effective and have high separation efficiency [40]. Hollow fiber membranes have already been used in the food industry, particularly in wine and beer clarification and in fruit juice filtration.

In the dairy industry, maximizing separation efficiency is crucial. Ceramic, polymeric spiral wound and hollow fiber membranes are affected by a casein rich fouling layer on the membrane surface due to the retention of casein during filtration [3,20,36,40]. The formation of the casein rich fouling layer is dependent on the flow characteristics in the membrane. Fouling in polymeric spiral wound membrane modules is highly influenced by the spacer geometry with the spacer strands causing an intense fouling, while in other areas it is less intense [14]. Hollow fibers have open, smooth channels and hence the fouling layer formation in these channels is more uniform. This difference in the fouling layer formation, thickness and compactness could potentially have an impact on the performance of the two membrane modules in terms of flux and transmission of serum protein. When transmembrane pressure is increased, the permeate flux increases, resulting in compaction of the fouling layer leading to an increase in steric resistance and a consequently a reduction in transmission of serum protein [27]. Further, the thickness of the fouling layer can be reduced by increasing the crossflow velocity [26]. For hollow fiber membranes this can be done without much consequence but in polymeric spiral wound membranes there are limitations, since this can results in structural instability

* Corresponding author.
E-mail address: anja.janssen@wur.nl (A.E.M. Janssen).

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due to critical back pressure that results in unwinding of the membranes module [18]. It is therefore crucial to assess and compare the filtration efficiency of the different membrane configurations.

Schopf et al. [40] compared the performance of ceramic, hollow fiber and polymeric spiral wound industrial sized modules of approximately one meter in length for fractionation of skim milk at 55 °C. The assessment was done with varying transmembrane pressures at the same feed volume and while the modules experience the same pressure drops. Hollow fiber performance was high enough to be considered as an alternative membrane configuration in the dairy industry [40]. They however, did not study the effect of concentration and diafiltration. Zulewska et al. [46] compared a uniform transmembrane pressure and graded permeability ceramic membrane with 0.1 μm pore size to a polymeric spiral wound membrane with 0.3 μm pore size. Skim milk was concentrated threefold at 50 °C. A higher serum protein yield was achieved with ceramic as compared to polymeric spiral wound membranes [46]. The flux of the spiral wound membranes was also significantly lower compared to that of the two ceramic membranes used. Hollow fiber membranes were not assessed in their study.

To further increase the efficiency of the membrane separation process concentration and diafiltration are incorporated. Preconcentration before diafiltration is a customary practice in the dairy industry. Both preconcentration and diafiltration are part of a multistep process that is beneficial in increasing the filtration efficiency which is not achievable with a single step [1,7,8,12,22,28,33,35]. In a skim milk multistep filtration process, diafiltration utilizes a diafiltration medium of known concentration to wash out the serum proteins that are not removed during the initial preconcentration process [5,10]. It is usually conducted in either batch or continuous mode. Diafiltration is especially important as it enhances the purities of retentate and permeate [8,9]. The amount of the serum protein removed from the feed increases and a purer casein rich retentate is achieved. The type of the diafiltration media also plays a crucial role in the separation efficiency.

Hartinger and Kulozik [13] investigated the effect of continuous diafiltration mode during skim milk fractionation using polymeric spiral wound membrane with a pore size of 0.1 μm at a temperature of 10 °C. In this investigation, they used permeate from ultrafiltration of skim milk (PUF) as the diafiltration medium. The beta-lactoglobulin (beta-lg)-to-casein ratio increased with the concentration factor [13]. Permeate fluxes remained stable during diafiltration regardless of the concentration factor used (1–4). The use of other diafiltration media or diafiltration modes was not investigated. Schopf and Kulozik [38] used a similar approach but instead used hollow fiber membranes. Eighty percent of the serum protein was removed using 2.5 diafiltration cycles and a concentration factor of 2.5, which was considered the optimum at 0.5 bar of transmembrane pressure and one bar of pressure drop [38]. Heidebrecht and Kulozik [15], investigated the use of continuous diafiltration using PUF and ceramic tubular membranes with a pore size of 0.14 μm at 50 °C. The transmission of serum protein was 55 % for the smallest protein, alpha-lactalbumin (alpha-la), and 50 % for beta-la; 90 % yield of immunoglobulins was achieved within the first 160 min of filtration [15]. However, denaturation of beta-la for up to 5 % was observed due to the long exposure to elevated temperatures. In these three studies the effect of batch diafiltration was not investigated and other diafiltration media were not used.

Reitmaier et al. [31] investigated the effect of diafiltration media (PUF, reverse osmosis water, tap water, and softened water) on casein micelle characteristics, fouling layer properties and separation properties during milk fractionation. Ceramic membranes were used at 50 °C and an increase in flux levels and separation was obtained with reverse osmosis water, due to the hydration of the fouling layer [31]. Tap water and softened water induced the least changes on the fouling layer. In the dairy industry, reverse osmosis water is the most common medium for diafiltration. This has been investigated using ceramic graded permeability membranes at 50 °C using concentration factor of three and polymeric spiral wound membranes at 24 °C and a concentration factor of four [24,43]. These studies showed that the permeate flux increases with increase in diafiltration, as confirmed by [23,25] [23,25]. The transmission of serum protein and the purity of the casein in the retentate increased with more diafiltration cycles. The findings were confirmed by [11]. The increase in permeate flux due to reverse osmosis water has been attributed to swelling of the casein micelles in the fouling layer further, increasing the interstitial spaces between the micelles, making the layer more permeable. These studies showed that reverse osmosis water is suitable diafiltration medium during milk protein fractionation. However, the operation temperature was high.

Despite extensive research on microfiltration based milk protein fractionation with diafiltration, systematic investigations of skim milk microfiltration in batch diafiltration mode using hollow fiber and spiral wound membranes at low temperature (10 °C) remain absent. In particular, these two configurations have not been compared especially when using reverse osmosis water as the diafiltration medium. This gap is critical, as both operating temperature, diafiltration medium, and membrane design strongly affect the selectivity of the membrane, energy requirements and process scalability. In this paper, we present the first direct comparison of these two membrane configurations when operated at 10 °C, focusing on their ability to fractionate casein from serum proteins. By explaining the relationship between operation mode and module architecture, this work delivers new insights which are useful for optimizing membrane based protein separation for advancing more efficient, scalable, and high-quality fractionation technologies. We therefore use results obtained on pilot scale to mimic the expected results in a larger industrial process where 200,000 l of skim milk is filtered within 20 h of operation. The yield of serum protein is maximized through preconcentration and diafiltration using reverse osmosis water.

2. Materials and methods

2.1. Materials

Pasteurized skim milk in 1 l batches was sourced locally from FrieslandCampina BV, The Netherlands, through one of their distributors (Jumbo Supermarket). The milk was stored at 4 °C for four days at most before being used in experiments. All experiments of skim milk fractionation were performed at 10 °C and at a pH of 6.8.

Two membrane configurations (spiral wound (SW) and hollow fiber (HF) membranes) were used. The spiral wound module made of polyethersulfone (PES) with a nominal pore size of 0.1 μm, 1 m in length, 4.6 m^2 membrane area and a 31 mil spacer was purchased from Koch Membrane Systems, Massachusetts, USA. This membrane was further reconfigured into 0.3 m length modules with a diameter of 0.046 m, an active area of 0.3 m^2, a 31 mil spacer and the pore size retained at 0.1 μm by Solsep BV, Apeldoorn, The Netherlands. The hollow fiber module was provided by Pentair-X-Flow, Enschede, The Netherlands. This membrane is made of polyethersulfone (PES) with a nominal pore size of 0.1 μm and an inner and outer diameter of fibers of 1.5 mm and 2.35 mm respectively, length of 750 mm and area of 0.1 m^2 according to the manufacturer's specifications. Hollow fiber membranes are operated in inside-out filtration mode. In each hollow fiber module, forty fibers were enclosed in a polysulfone (PSU) tube, with the entrance and the exit of the modules covered in potting approximately 25 mm length. This length did not contribute to the active filtration area.

2.2. Membrane filtration system

Spiral wound microfiltration was performed using a pilot scale membrane filtration unit as described by (Aguirre Montesdeoca et al., 2016b; [34]). The unit was equipped with a plate heat exchanger for temperature control at the desired temperature (10 °C). Hollow fiber microfiltration experiments were performed using a pilot scale filtration unit which was equipped with a frequency regulated centrifugal pump

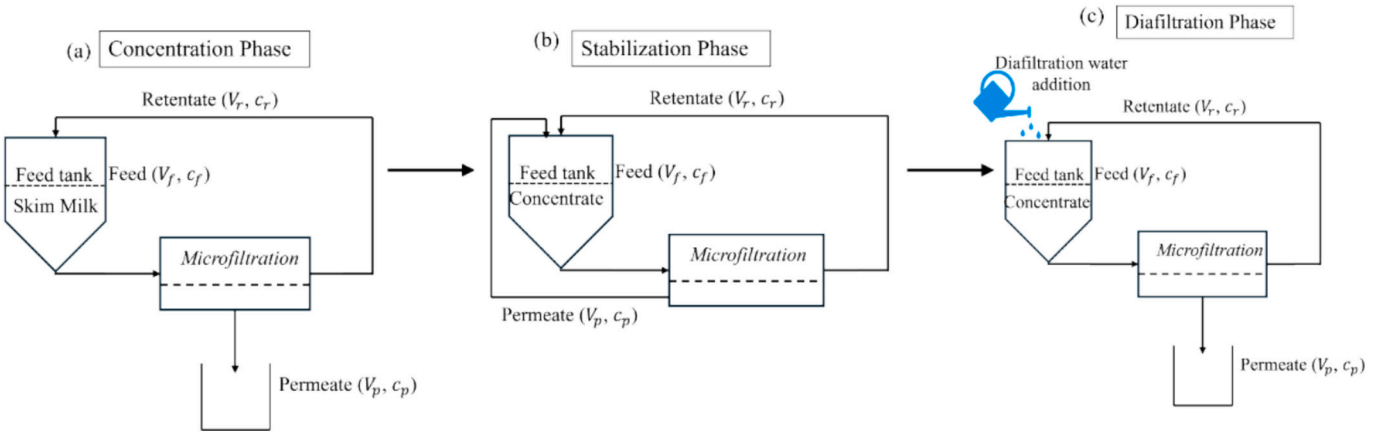

Fig. 1. Schematic representation of the filtration process where (a) shows the concentration process, (b) shows the stabilization process to achieve steady state and (c) shows the diafiltration process where a known volume of water is added to the feed tank containing the concentrated milk.

(CSF Inox, Montecchio E. Italy). The temperature was controlled by a double-walled feed tank connected to a heat exchanger that circulated temperature-controlled water through the tank jacket. The pressures of the feed, retentate and permeate were registered using digital pressure transmitters (Cerabar T, Endress and Hauser, Germany). The flow volume was recorded using volumetric flow meters (Es-Flow, Bronkhorst, UK).

2.3. Conditioning and cleaning procedure

2.3.1. Pilot scale installation equipped with SW membranes

After flushing out any residual skim milk in the pilot scale installation with water, an enzymatic cleaning was conducted using a solution of Divos 90 at 1 % (v/v) and Divos 80–2 at 0.35 % (v/v) respectively. This solution was recirculated for 40 min at a temperature of 50 °C. Rinsing was done using tap water to a neutral pH at a temperature not higher than the cleaning temperature. Acidic cleaning followed by using Divos 2 at 0.5 % (v/v) for 20 min at a temperature of 50 °C. This was followed by rinsing using tap water until neutral pH is achieved. The last step was alkaline cleaning using Divos 116 at 0.8 % (v/v) for 25 min at 50 °C. After rinsing out the alkaline cleaning compound, a clean water flux experiment was conducted using demineralized water to assess the effectiveness of cleaning. All Divos cleaning agents were purchased from Diversey, The Netherlands.

2.3.2. Pilot scale installation equipped with HF membranes

After each hollow fiber filtration experiment, the membrane module and the pilot unit were cleaned separately. The membrane module was cleaned with an enzymatic agent (0.3 % v/v Ultrasil 67, Ecolab Deutschland GmbH, Germany) and a caustic agent (0.1 % v/v Ultrasil 69, Ecolab Deutschland GmbH, Germany) at 50 °C for 40 min. Finally, an acidic agent (HNO_3 at a pH of 2) was used at 50 °C for 35 min. The pilot unit was rinsed with water and then cleaned with caustic (NaOH 33 % v/v) at 50 °C. Finally, all the water in the system was flushed out using pressurized air. Before starting any experiments, the membrane modules were rinsed with reverse osmosis water for 15 min and their clean water flux checked to ensure that the membrane modules were thoroughly cleaned.

2.4. Experimental design

All experiments were performed in duplicate using different batches of skim milk. For experiments with spiral wound membranes, a maximum of 10 l of skim milk was used as the feed volume. With the hollow fiber membranes installation a maximum of 20 l of skim milk was used as feed volume. The feed volume used for filtration was determined prior to the experiment based on the volume reduction factor being investigated. At the start of filtration, the milk was conditioned to 10 °C in the feed tank after which the filtration was started at the desired crossflow velocity and transmembrane pressure. Monitoring of the experiments was done to avoid any back pressure; only positive transmembrane pressures along the length of the membrane modules were achieved. Filtration in concentration and diafiltration mode was adopted for both SW and HF membrane experiments as follows:

2.4.1. Filtration in concentration mode

With both the SW and HF modules, the crossflow velocity was kept constant at 0.16 m/s and 1.5 m/s respectively and transmembrane pressure ranging from 0.42 to 0.96 bar. The skim milk was recirculated in the system for 30 min to achieve a steady state. The milk was then concentrated by draining out the permeate stream to achieve a specified volume reduction factor (VRF) from known initial feed volume (V_{feed}) to a final volume of the retentate at the end of pre-concentration ($V_{end\ of\ pre-concentration}$) as shown in Fig. 1 (a). The VRF was calculated as initial feed volume divided by final retentate volume obtained at the end of pre-concentration. We conducted experiments, taking samples at the beginning of concentration and the end of concentration for both configurations.

2.4.2. Filtration in diafiltration mode

After the pre-concentration step, diafiltration was performed on the concentrated milk in batch diafiltration mode. RO water was used as diafiltration medium and supplied to the concentrated retentate in the feed tank at a volume equal to the amount of permeate drained during pre-concentration to achieve a similar initial volume as before the start of pre-concentration. The RO water is added in batches in the feed tank at a temperature of 10 °C. The mixture of RO water and concentrated milk was then recirculated in the filtration loop for 30 min for effective mixing and to achieve steady state as shown in Fig. 1 (b). After achieving a steady state, a permeate volume equal to the amount of RO water added was then drained and the cycle was repeated four times as shown in Fig. 1 (c). Each of these cycles is referred to as a diafiltration cycle (DF cycles).

During all the above experimental routes, retentate and permeate samples were taken for further analysis using High Performance Size Exclusion Chromatography (HPSEC).

2.5. Determination of the concentration of milk proteins

The analysis of the concentrations of casein and serum protein (sum of beta-lg, alpha-la and IgM) was done using High Performance Size Exclusion Chromatography (HPSEC), using two columns in series

namely TSK G400SWxl 7.8 × 300 mm, eight µm and TSK 53000SWxl 7.8 × 300 mm, five µm by Tosoh Bioscience. The mobile phase applied consisted of 0.01 % Trifluoroacetic acid (TFA) in 69.9 % High Performance Liquid Chromatography (HPLC) grade water and 30.0 % Acetonitrile (ACN). The flow rate was 1.5 ml/min, the column temperature was kept at 30 °C and detection was done at a UV wavelength of 215 nm. For the analysis of the serum proteins, the casein was precipitated by adding 4 M hydrochloric acid and centrifugating at 4000 g for 10 min at a temperature of 20 °C. The supernatant was then analyzed using the abovementioned columns, eluents, and operation conditions.

2.6. Calculation of characteristics of microfiltration process

The flux, $J\left(lm^{-2}h^{-1}\right)$, is calculated as a function of the permeate flow rate $Q_p\left(lh^{-1}\right)$ and the active membrane area, $A_m\ (m^2)$ as Eq. (1.1):

$$J = \frac{Q_p}{A_m} \tag{1.1}$$

The average flux $J_{average}$ achieved during preconcentration and diafiltration at a target concentration level is defined according to Eq. (1.2):

$$J_{average} = \frac{J_{initial} + J_{final}}{2} \tag{1.2}$$

The transmission of milk protein i (T_i) was determined as a function of the concentration in the permeate $c_{i,p}\left(gl^{-1}\right)$ and retentate $c_{i,r}\left(gl^{-1}\right)$ as Eq. (1.3). The relationship of transmission to rejection (R_i) is also shown in eq. (1.3):

$$T_i = \frac{c_{i,p}}{c_{i,r}} \times 100 = 100 - R_i \tag{1.3}$$

The mass flow of protein I, $M_J\ \left(gm^{-2}h^{-1}\right)$ was calculated as a function of the permeate concentration in the permeate $c_{i,p}\left(gl^{-1}\right)$ and the flux (J) experienced by the membrane at a specific transmembrane pressure of evaluation as Eq. (1.4):

$$M_J = c_{i,p} \times J \tag{1.4}$$

The (average) transmembrane pressure ($TMP\ (bar)$) used was calculated as Eq. (1.5):

$$\text{Transmembrane Pressure (TMP)} = \left(\frac{P_f + P_r}{2}\right) - P_p \tag{1.5}$$

where P_f, P_r, and P_p are feed, retentate and permeate pressures in bar.

The volume reduction factor (VRF) was calculated as the ratio of the initial feed volume $V_f(l)$ and the final volume of retentate after preconcentration ($V_r(l)$) as Eq. (1.6):

$$VRF = \frac{V_f}{V_r} \tag{1.6}$$

The purity of the protein in the permeate for serum protein and in the retentate for casein was calculated with Eq. (1.7):

$$\text{Purity} = \frac{c_{i,p,r}}{\sum c_{j,p,r}} \tag{1.7}$$

where $c_{i,p,r}$, is the permeate or retentate concentration of one protein and $\sum c_{j,p,r}$ is the sum of the permeate or retentate concentration of all proteins present. The yield of serum proteins in the permeate was calculated as a function of the volume of feed (V_f), volume of permeate (V_p) in liters, concentration of in the permeate $\left(c_{i,p}\left(gl^{-1}\right)\right)$ and feed $\left(c_{i,f}\left(gl^{-1}\right)\right)$. Yield (Y_{sp}) is calculated for all components i and n represents the number of cycles (pre-concentration and diafiltration cycles). The concentration of permeate used for the calculation of yield is the total concentration of the collected permeate during each diafiltration cycle. Recovery of casein (Re_{cn})in the retentate is calculated as a function of volume of the retentate (V_r) in liters, volume of the feed (V_f) in liters, concentration of casein in retentate $\left(c_{i,r}\left(gl^{-1}\right)\right)$, and concentration of casein in the feed $\left(c_{i,f}\left(gl^{-1}\right)\right)$.

$$Y_{sp} = \frac{\sum_0^n V_p c_{i,p}}{V_f c_{i,f}} \tag{1.8}$$

$$Re_{cn} = \frac{\sum_0^n V_r c_{i,r}}{V_f c_i} \tag{1.9}$$

3. Parameter fitting

3.1. Preconcentration phase

Milk protein concentrations in the retentate and permeate were estimated with component balances for a filtration system with a filtration capacity of 200,000 l of skim milk in 20 h using eq. (1.10). V_f is the feed volume in liters, V_r is the retentate volume in liters, and V_p is the permeate volume in liters. c_f, c_r, and c_p are the concentrations of proteins $\left(gl^{-1}\right)$ in the feed, retentate and permeate stream respectively [35].

$$V_f c_f = V_r c_r + V_p c_p \tag{1.10}$$

Additionally, the c_p can be expressed in respect to c_r and rejection (R) of each milk protein of interest as per eq. (1.11):

$$c_p = c_r(1 - R) = c_r T \tag{1.11}$$

When eq. (1.6) and (1.11) are substituted in eq. (1.10), eq. (1.12) is achieved (see Supplementary material A1).

$$c_r = \frac{VRFc_f}{1 + (VRF - 1)(T)} \tag{1.12}$$

The yield of serum protein in the permeate can further be determined using eq. (1.13). The derivation of eqs. (1.13) can be seen in Supplementary material A2.

$$Y_{i,n} = 1 - \left(\frac{1}{1 + (VRF - 1)(T)}\right) \tag{1.13}$$

where $Y_{i,n}$ is the yield of component i in n step.

3.2. Diafiltration phase

The performance of batch diafiltration is explained in section 1.2.4.2. During this process, the concentration in the retentate changes. Several cycles of application of diafiltration water (m) can be used. The effect on the retentate concentration $(c_{r,i,n})$ can be described as follows [45]:

$$c_{r,i,n} = c_f\left(\frac{V_0}{V_d}\right)^{1-T}\left(\frac{V_d}{V_d + V_w}\right)^{m-1}\left(\frac{V_d}{V_d + V_w}\right)\left(\frac{V_d + V_w}{V_0 - V + mV_w}\right)^{1-T} \tag{1.14}$$

where c_f (gl^{-1}) is the concentration in the retentate at the end of preconcentration phase, V_0 (l) is the initial volume of the feed, V_d (l) is the volume of retentate at the end of pre-concentration, V_w (l) is the volume of diafiltration water added, V (l) is the volume of the filtrate, and T is the transmission of each protein being evaluated. The transmission T is calculated as concentration in the permeate divided by concentration in the retentate. At the end of diafiltration, the final retentate concentration can be calculated as [45]:

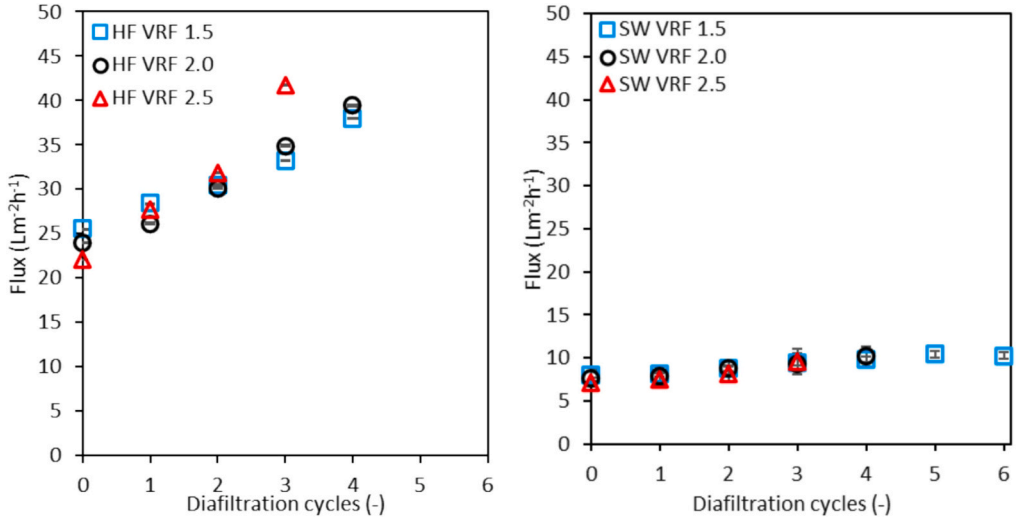

Fig. 2. Graph on the left shows the average flux obtained during preconcentration (0) phase and during diafiltration of four cycles for different VRFs using hollow fiber membrane (HF) at 0.5 bar of transmembrane pressure. Graph on the right shows the resulting average flux during preconcentration (P) phase and six diafiltration cycle for spiral wound membranes (SW) at 0.5 bar of transmembrane pressure. Preconcentration was performed as section 1.2.4.1 and batch diafiltration was described in section 1.2.4.2. The average flux was calculated using eqs. 1.1 and 1.2.

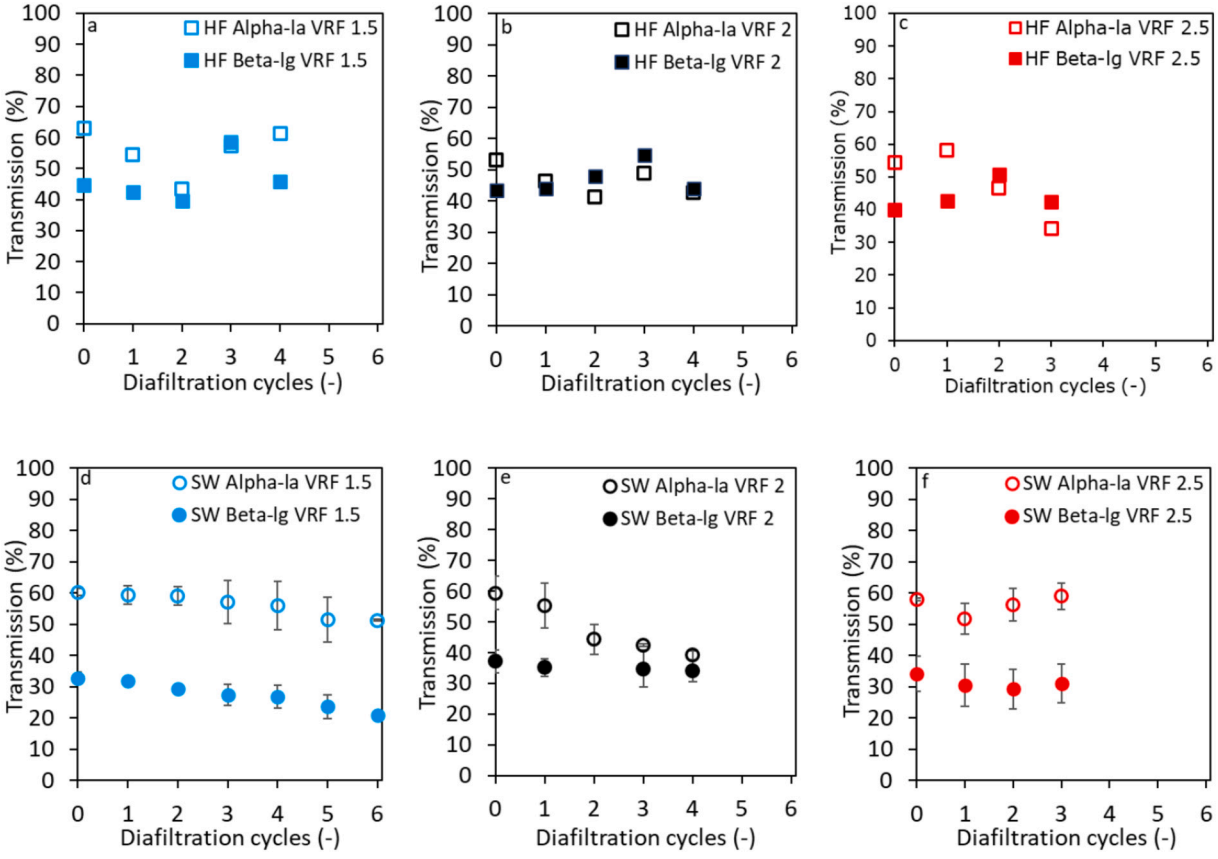

Fig. 3. Transmission of beta-lg (solid dots and squares) and alpha-la (empty dots and squares) for both hollow fiber (HF) (graphs a, b, c) and spiral wound (SW) membranes (graphs d, e, f) during preconcentration (denoted by 0) and diafiltration phase (diafiltration cycles 1 to 6) as stipulated in section 1.2.4.1 and 1.2.4.2. Transmission is calculated according to eq. 1.3. The experiments were conducted at 0.5 bar of transmembrane pressure. The transmissions are calculated at the end of the diafiltration cycles. The error bars for hollow fiber membranes is small hence not visible.

$$c_{r,i,n} = c_f \left(\frac{V_e}{V_0}\right)^{T-1} \left(1 + \frac{V_w}{V_d}\right)^{-nT} \tag{1.15}$$

where V_e (l) is the volume of the retentate at the end of the diafiltration process and n is the total number of diafiltration cycles used through out the diafiltration process. The yield of the serum proteins (Y_i) obtained at the end of the diafiltration process can also be calculated using the following equation [45]:

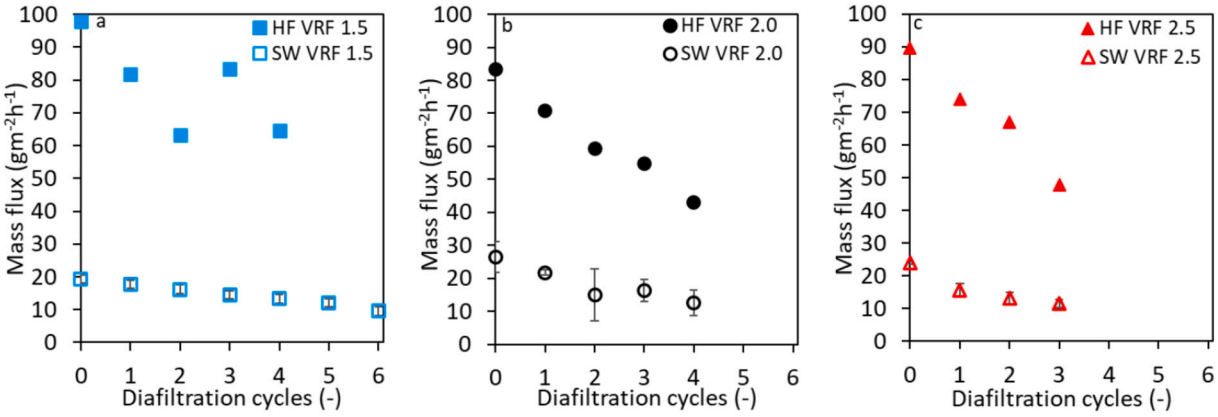

Fig. 4. Mass fluxes of serum protein for preconcentration (denoted by 0 on the x axis) diafiltration cycles. This is shown for hollow fiber (solid icons, HF) and spiral wound membrane (empty icons, SW) configuration and for different VRFs. The mass fluxes are calculated using eq. 1.4. Blue squares, black dots and red triangles represent VRF 1.5, 2.0, and 2.5 shown in graphs a, b, and c, respectively. The error bars for hollow fiber membranes is small hence not visible. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

$$Y_i = 1 - \left[\frac{V_e}{V_0}\left(1 + \frac{V_w}{V_d}\right)^{-n}\right]^T \tag{1.16}$$

The membrane area $A_m(m^2)$ can further be calculated using the volume of the permeate $V_p\ (l)$, the achievable permeate flux $J\ (lm^{-2}h^{-1})$, the operation time $t\ (h)$ and the feed volume $V_f\ (l)$. The volume of permeate is the difference between the initial feed volume and retentate volume. The retentate volume for each VRF is calculated using eq. 1.17. Membrane area is also affected by the operation period as seen below.

$$A_m = \frac{V_p}{J \times t} = \frac{V_f Y_i}{J \times t} \tag{1.17}$$

3.3. Data and statistical analysis

The standardization of the data is done based on the membrane area to ensure even comparison between two membrane modules of different membrane area especially in flux and mass flux comparison. Key performance indicators such as transmission expressed as a percentage, yield and purity expressed as ratios are ensured to have similar units, scale and magnitude. Analysis of variance (ANOVA) was used to determine whether differences in a particular set of measured parameters were statistically significant. Data shown are averages of the results obtained from two independent filtration experiments with error bars showing the absolute difference between two sets of experiments.

4. Results and discussion

4.1. Average flux during preconcentration and diafiltration

The average fluxes during preconcentration and diafiltration for both hollow fiber and spiral wound membranes are shown in Fig. 2. Using hollow fiber membranes, VRF 1.5 gave the highest flux of 25 $lm^{-2}\ h^{-1}$ during the preconcentration phase while VRF 2.5 gave the lowest flux of 22 $lm^{-2}\ h^{-1}$ (Fig. 2 left). This trend was maintained until the third diafiltration cycle where VRF 2.5 resulted in a higher average flux; however, the differences are not large. The average flux increased with the number of diafiltration cycles. Spiral wound membranes (Fig. 2 (right)) behaved similarly to the hollow fiber membranes, but the average flux was lower. For the spiral wound membrane, VRF 2.5 gave the lowest flux until the second diafiltration cycle while an equal flux observed with the third diafiltration cycle. Again, the differences are small and considered insignificant (p-value = 0.093).

The increase of the flux subsequent to diafiltration cycles is mainly due to the decrease in feed viscosity. The concentration of serum protein has little to no effect on the viscosity of the feed as compared to the effect of lactose: the lactose concentration is eight times higher than that of the serum proteins combined [11].

During diafiltration, lactose is quickly washed out of the feed. This decrease in lactose concentration in the retentate results in a decrease in viscosity which promotes diffusional mass transfer in the membrane channels resulting in an increase in flux. Next to that, use of reverse osmosis water leads to modification of the casein micelle properties as the lower osmotic pressure from the water results in dissolution of the calcium phosphate nanocrystals, swelling of the micelles and higher permeability of the accumulated layer. This also increases the resulting permeate flux. Granger-Delacroix et al., [11] demonstrated the solubilization of the phosphates from the micelles to the serum phase during diafiltration of skim milk using reverse osmosis water at 12 °C. This was further confirmed by Li and Corredig [21] and Alexander et al. [2] who showed partial solubilization of micellar calcium during ultrafiltration of skim milk to VRF 2.5 and diafiltration using reverse osmosis water for 2.5 to 5 diafiltration cycles [2,21].

4.2. Transmission of serum protein and casein during preconcentration and diafiltration process

The transmission of beta-lg with hollow fiber membranes was constant during preconcentration and diafiltration with a slight increase in the second and third diafiltration cycle (fig. 3) followed by a decrease in the transmission. We observed a beta-lg transmission of 44 %, 42 % and 40 % for VRF 1.5, 2.0 and 2.5 respectively with hollow fiber membranes during preconcentration. For spiral wound membranes, the transmission of beta-lg during preconcentration was 32 %, 37 %, and 35 % for VRF1.5, 2.0 and VRF 2.5. For spiral wound membranes, the transmission of beta-lg was constant except for VRF 1.5 at which a decrease in transmission was observed. The transmission was slightly lower than that of the hollow fiber membranes. The fouling layer on hollow fiber membranes is assumed to accumulate more beta-lg as compared to that of spiral wound membrane; the release of this accumulated beta-lg then causes an increase in the transmission before a decrease starts which is assumed to be caused by depletion of beta-lg in the fouling layer. The structure of the membrane is also hypothesized to have an effect on the transmission since the manufacturing of these two membranes is different even though the polymer used is similar. The distribution of pores could further be different further affecting the transmission.

The transmission of alpha-la has variation over the diafiltration cycles for both membranes. The reason for the difference in trend with alpha-la as compared to that of beta-lg is due to its conformational structure, which depends on the presence of a calcium moiety, as it is a metalloprotein [11]. The change in ionic strength and solubilization of

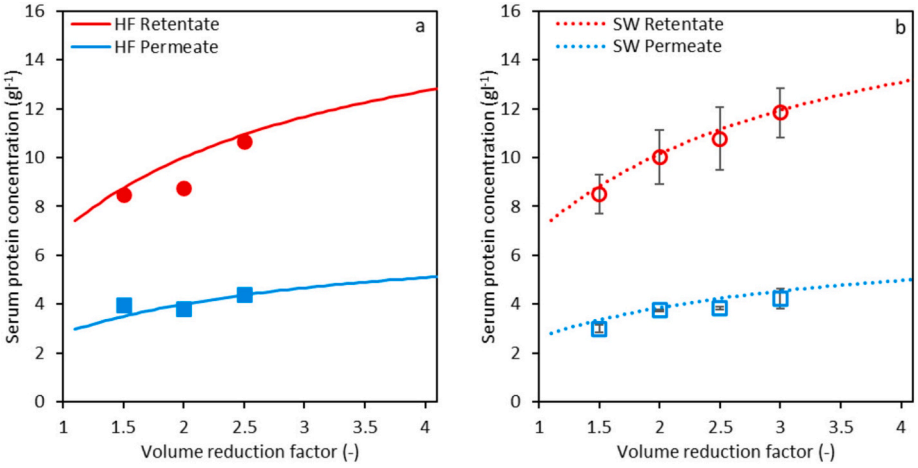

Fig. 5. The graph (a) shows the results of the calculated retentate (red) and permeate (blue) concentrations for the pre-concentration process done using hollow fiber (HF) membranes (solid lines). Graph (b) shows the calculated retentate (red) and permeate (blue) concentrations for pre-concentration process done using spiral wound (SW) membranes (dotted lines) using Eqs. (1.11) and (1.12). Additionally the retentate and permeate concentration data obtained during experiments as shown in section (1.2.4.1), are shown where solid and empty red dots and solid and empty blue squares represent retentate and permeate experimental results conducted using hollow fiber (HF) and spiral wound (SW) membranes respectively. The error bars for hollow fiber membranes is small hence not visible. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

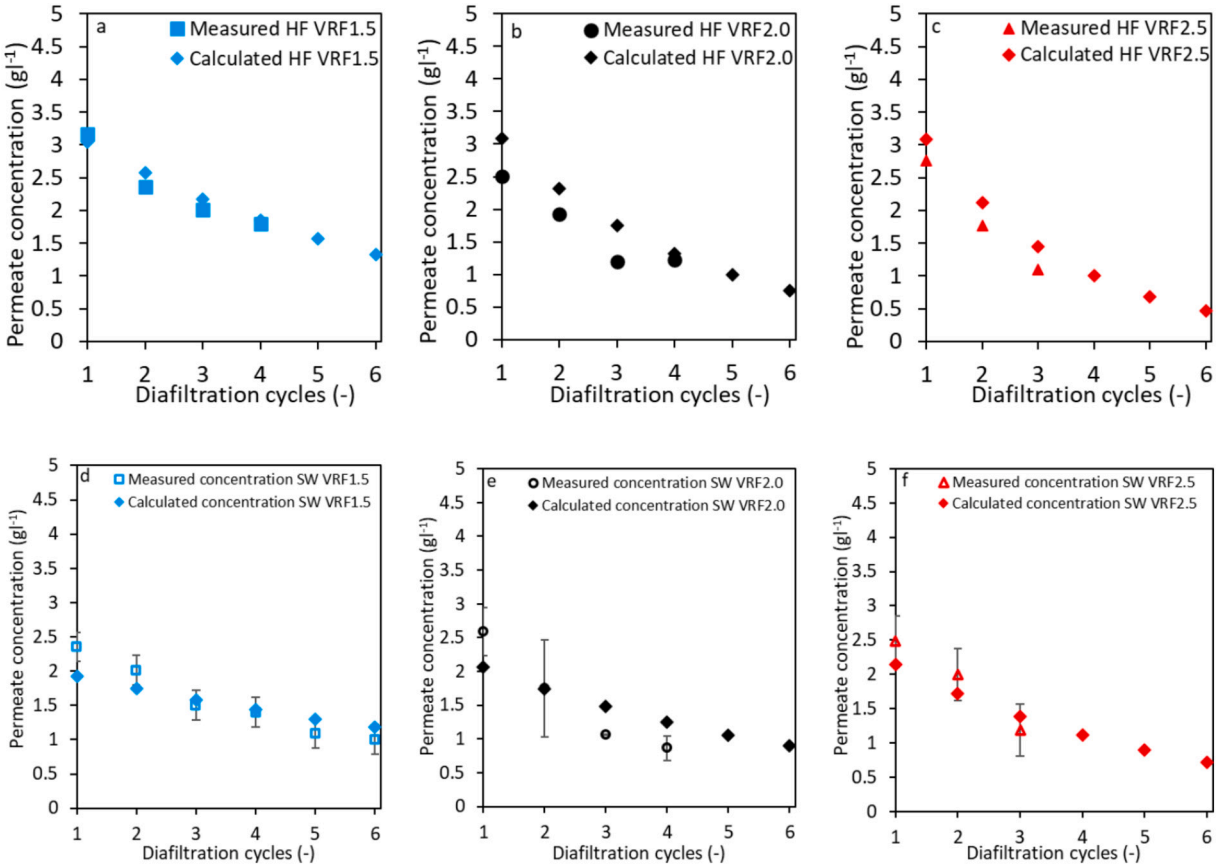

Fig. 6. Concentration of serum protein in the permeate during batch diafiltration with six diafiltration cycles for hollow fiber membranes graphs a. b and c and for spiral wound membranes graphs d, e, and f the concentrations are calculated using eq. 1.11 with the retentate concentration in eq. 1.11 calculated using eq. 1.14. Blue, black, and red represent VRF 1.5, 2.0 and 2.5 respectively. The serum protein concentrations were measured at the end of the diafiltration cycles. The error bars for hollow fiber membranes is small hence not visible. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

encapsulated calcium ions changes the conformation of alpha-la [11]. This changes the interaction between casein and alpha-la and this interaction will be different from that of beta-lg to casein. The transmission of casein increases over the diafiltration cycles (see Supplementary material Fig. A1) with the spiral wound module giving higher transmission of 1 % during preconcentration and 2 % during

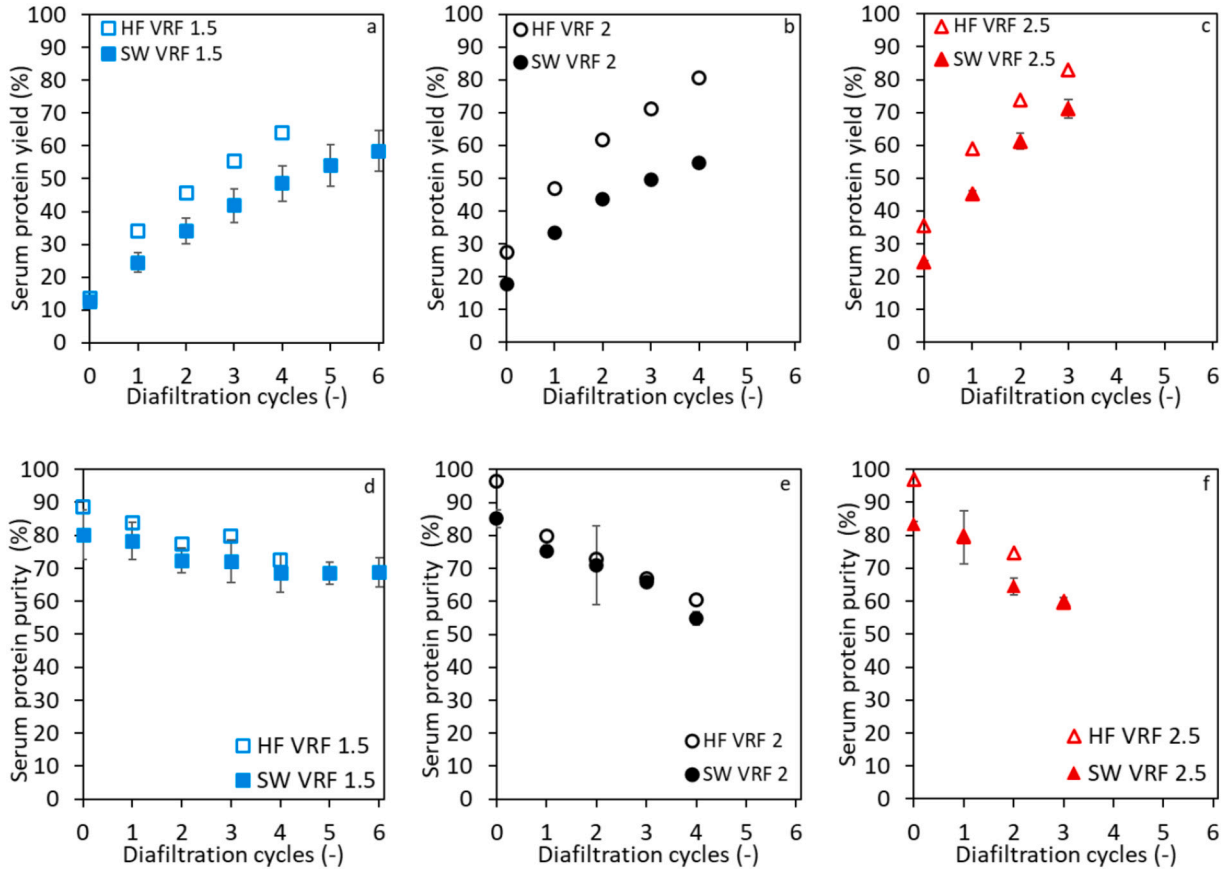

Fig. 7. The serum protein yield (a, b, c) and purity (d, e, f) for both spiral wound (sw) and hollow fiber (hf) membranes in respect to number of diafiltration cycles starting from preconcentration denoted by 0 on the x axis is shown in the graphs for different volume reduction factors. Graph a, b, c represents serum protein yield for VRF 1.5, 2, and 2.5 respectively and d, e, f represents serum protein purity for VRF 1.5, 2, and 2.5 respectively. The data presented is based on experimental results and calculated using eq. 1.8 for both hollow fiber and spiral wound membranes and for both preconcentration and diafiltration. Calculation of yield is done using the concentrations of the cumulative permeate collected during each diafiltration cycle. The error bars for hollow fiber membranes is small hence not visible.

diafiltration. The hollow fiber modules on the other hand give lower transmissions starting from 0.5 % during preconcentration to 1 % during diafiltration.

Additionally, the spiral wound membrane module used was 0.3 m in length which is significantly shorter than the hollow fiber membrane module (0.75 m). It has been shown that length has an effect on the filtration performance of membrane modules. Hartinger et al. (2019) investigated the influence of length on transmission of beta-lg and casein where a 0.96 m spiral-wound membrane module as a whole and another one divided into four sections. A reduction in overall transmission for membranes with larger length (whole module) was observed. This was also observed with hollow fiber and ceramic membranes [29,30,39]. Nyambura et al., 2025, compared different lengths of hollow fiber membranes (0.3 and 0.75 m), and the longer module could not achieve higher transmissions due to higher pressure drops experienced. The higher pressure drops results in increase in transmembrane pressure which negatively affect transmission [26]. This shows that spiral wound membrane in our study, due to its shorter length has a performance advantage but still hollow fiber membranes perform better than spiral wound membranes.

4.3. Effect of membrane configuration on the serum protein mass fluxes during preconcentration and diafiltration process

To further compare hollow fiber and spiral wound membranes, the serum protein mass fluxes can be used. The mass flux of a solute indicates the amount of solute obtained per given filtration period and membrane area. Here, the overall serum protein concentration is taken as the sum of the concentrations of beta-lg, alpha-la, IgM, and IgG. From Fig. 4, we observe that the serum protein mass fluxes for both configurations decrease with the number of the diafiltration cycles. The hollow fiber membrane has higher mass fluxes than the spiral wound membrane, due to the higher serum protein concentration in the permeate.

The higher permeate concentration paired with higher fluxes during preconcentration and diafiltration for hollow fiber membranes results in higher mass fluxes. The mass flux for hollow fiber membrane at VRF 1.5 is fivefold that of spiral wound membranes, due to the vastly different hydrodynamics. Hollow fiber membranes are operated at a higher crossflow velocity leading to a thinner concentration polarization layer and higher fluxes, and hence higher concentrations in the permeate.

4.4. Effect of membrane configuration on serum protein concentration in the retentate and permeate during preconcentration and diafiltration

Through the mass balances and eqs. 1.12 and 1.13, the concentrations of the serum proteins in the permeate and retentate were calculated. The concentration in the feed at the beginning of the filtration sequence is taken to be the concentration of protein in skim milk (35 and 7 g/l for casein and serum protein respectively). The retention used in eqs. 1.12 and 1.13 is 0.6 and 0.62 for hollow fiber and spiral wound membranes respectively (see section 1.4.2). These retentions were obtained from the experimental measurements. Fig. 5 shows that the concentration f serum protein in the retentate and permeate increases with the VRF. Both membrane configurations give similar concentrations in the retentate and a slight difference in the permeate concentrations. During pre-concentration, the thickness of the fouling layer on

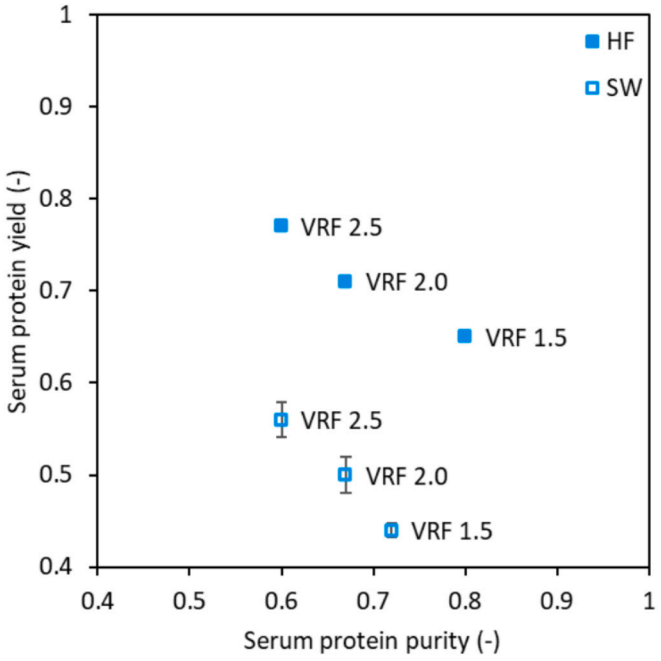

Fig. 8. Serum protein yield with respect to the purity obtained during diafiltration experiments with three diafiltration cycles. Three VRFs, namely 1.5, 2.0, and 2.5 are investigated. Overall yield and purity are calculated using 1.16 and 1.7, respectively. The error bars for hollow fiber membranes is small hence not visible.

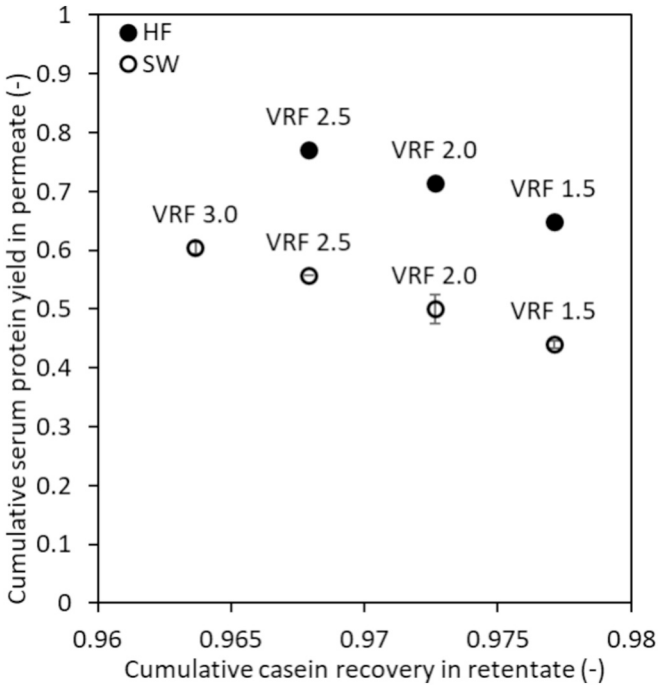

Fig. 9. The graph shows the relationship between the cumulative yield of serum protein in the permeate and cumulative recovery of casein in the retentate when three diafiltration steps are applied based on experimental data using eq. 1.8 and 1.9. The error bars for hollow fiber membranes is small hence not visible.

the membrane surface increases with the VRF. The formation and behavior of this layer will be similar above the critical transmembrane pressure, which is approximately 0.25 bar: much lower than the experimental transmembrane pressure (0.5 bar). At transmembrane pressures above the critical transmembrane pressure, micelles accumulate on the membrane surface and the space in between these micelles affect the retention due to size exclusion [27]. Since the size of these pores is smaller than the diameter of the casein micelles, it results in almost 100 % retention of micellar casein and significant transmission of the serum proteins due to the size differences. An increase in the retentate concentration is not expected to influence the interstitial spaces between the micelles, as these depend on the pressure gradient over this micellar layer.

The operational transmembrane pressure is not changed and hence the deformation of the micelles is not changed. Thus, the serum protein concentrations in the permeate are almost equal for both membrane configurations. Other mechanisms such as dielectric exclusion are suspected to contribute to a lower serum protein concentration in the permeate. Similar behavior was observed with the results of casein concentration in the retentate and permeate (see Supplementary material Fig. A2).

During diafiltration, the retentate concentrations obtained with the preconcentration step were used as the feed concentration for each specific volume reduction factor used during experiments. Fig. 6 shows that the overall concentration of serum proteins in the permeate decreases with the diafiltration cycles for both membrane configurations. However, the hollow fiber membrane gives slightly higher permeate concentrations and there is also a sharper decline in the concentration from preconcentration to the start of diafiltration in hollow fiber membrane as compared to that of spiral wound membranes. This is due to higher yield of the serum protein during preconcentration by hollow fiber membranes; a trend that is also observed during diafiltration (see Supplementary material Fig. A3).

The differences between the calculated and experimental values are due to the use of the averaged serum protein retentions at 0.6 and 0.62 for hollow fiber and spiral wound membranes, respectively. The difference accounts for the difference in permeate concentration. The highest difference was 0.5 g/l obtained at VRF2.0. The decrease in the concentration in the permeate is due to the reduction of the serum protein present in the retentate (see Supplementary material Fig. A4). As more diafiltration water is used past the fourth diafiltration cycle, the concentration of serum protein starts to level off when using spiral wound membranes at VRF 1.5 and compared to the calculated values. We hypothesize this to be due to higher solubilization of calcium phosphate into the serum phase, changing the properties of the fouling layer, and further limiting the transmission of the serum proteins.

4.5. *Yield and purity during preconcentration and diafiltration*

During preconcentration and diafiltration, a given volume of permeate with serum protein is removed to achieve a specified VRF using both hollow fiber and spiral wound membrane configurations and later diafiltration medium in this case reverse osmosis water is introduced to enhance the separation of proteins. During this process, the yield and purity of the permeate was assessed. Fig. 7 (a, b, c) shows a difference in the serum protein yield between spiral wound and hollow fiber membranes during preconcentration (denoted by 0 on the x axis in the graphs). In the preconcentration phase, the serum protein yield for hollow fiber membranes is higher as compared to the spiral wound membranes, except for VRF 1.5. An increase in yield with increase in diafiltration cycles was observed for both configurations. The serum protein yield during diafiltration is 1.2 to 1.5 times higher for the hollow fiber membranes as compared to the spiral wound membranes. The *p*-values for the comparison of yield are 0.009, 0.0087, and 0.001 for VRF 1.5, 2, and 2.5, respectively, showing significant differences.

Fig. 7 (d, e, f) shows that serum protein purity decreased with increase in diafiltration cycles. Difference in purity was mainly observed during preconcentration for all VRFs investigated. This is due to hollow fiber membranes having lower casein transmission during

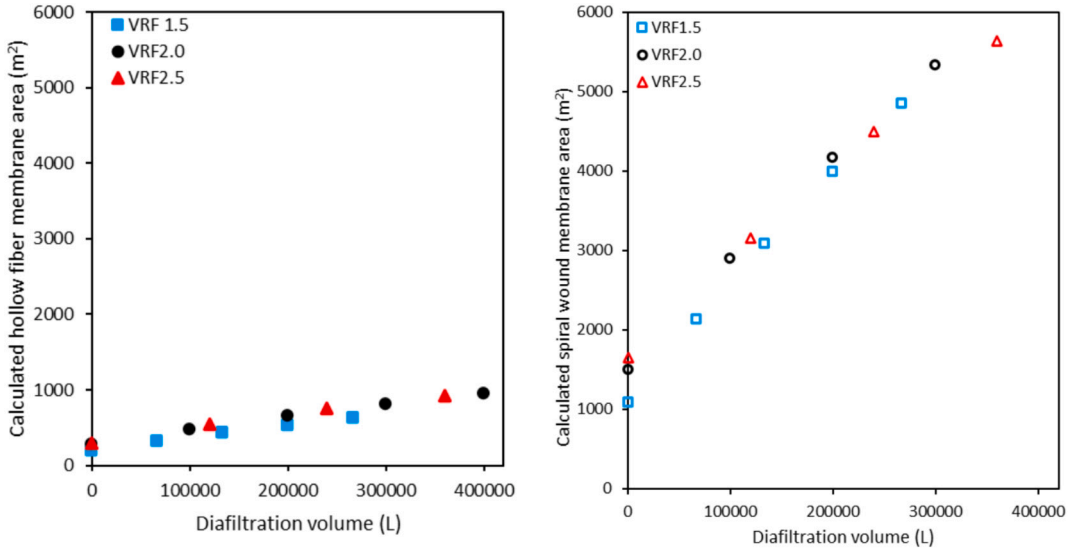

Fig. 10. The graphs show the required membrane area for different VRFs during diafiltration calculated using eq. 1.17. The graph (a) represents the calculated cumulative membrane area for hollow fiber membranes and (b) represents the calculated cumulative membrane area for spiral wound membranes. The specific membrane areas and diafiltration water volumes are shown in the Supplementary material Table A1.

preconcentration as seen in the supplementary material fig. A1. The contribution casein transmission in lowering the purity of serum protein is due to the depletion of salts present in milk. When the salts are washed out during diafiltration, the ionic strength is reduced causing the structure destruction of the casein micelles [4,11,31,32]. When the micelles structure is destroyed, the sizes of the micelles changes contributing to the higher transmission of casein which is further reducing the purity of serum protein in the permeate. Between the two configurations, the differences in purity during diafiltration were considered insignificant. The p-values for serum protein purity are 0.07, 0.06 and 0.159 for VRF 1.5, 2, 2.5, respectively, showing that the values are not significantly different. The differences in purity are not excessively large due to the loss of casein to the permeate for both configurations being comparable. Therefore, increasing diafiltration cycles not only increases the yield but also decreases the purity of the permeate further requiring a polishing step if total separation of milk proteins is desired.

Further, assessment of the differences between the configurations was done based on the overall performance of the membranes. Fig. 8 shows the result after three diafiltration cycles for the different VRFs investigated based on experimental data. The overall yield was calculated using eq. 1.16 and the purity at the end of the third cycle was calculated using eq. 1.7. Fig. 8 shows the performance of hollow fiber and spiral wound membrane. A decrease in purity and an increase in yield is found with volume reduction factors. Hollow fiber membranes show a better combination of yield and purity compared to spiral wound membranes. At VRF 2.5 a yield of 0.77 and with a corresponding purity of 0.60 is obtained. A spiral wound membrane at this VRF 2.5 results in a yield lower than 0.6.

4.6. Cumulative serum protein permeate recovery vs cumulative recovery of casein in retentate

The goal of the preconcentration and diafiltration steps is to recover the serum protein in the permeate and the casein in the retentate with yields and purities as high as possible. With three diafiltration cycles, the recoveries are calculated and shown in Fig. 9 based on the experimental data. An increase of the yield of serum protein permeate with the VRF is associated with decrease in the yield of casein: as more serum protein is washed out, more casein is washed with it as well. Fig. 9 also shows the differences between the hollow fiber and spiral wound membranes. The ideal outcome is to have high yields in both the retentate (casein) and permeate (serum proteins) (top right side of the graph). However, a better yield of serum protein negatively affects the casein protein yield especially with application of more diafiltration water.

4.7. Estimated membrane area required during preconcentration and diafiltration

Using the experimentally measured permeate flux and the expected permeate volumes (Fig. 2), the required membrane areas to process 200,000 l of skim milk were estimated (by using eq. 1.16). The membrane areas were calculated for yield of serum protein of 0.77 for both hollow fiber and spiral wound membrane. Fig. 10 shows that the cumulative membrane area increases with the increase diafiltration volume. The membrane areas required to achieve 0.77 serum protein yield are dependent on the amount of diafiltration water used during filtration. The spiral wound membrane system based on the slope of the data requires approximately 7 times more membrane area than hollow fiber membrane, due to the lower flux of spiral wound membranes compared to that of hollow fiber membranes. This difference is even higher if industrial scale membranes were to be used since, for longer modules the transmission of serum proteins would be lower hence requiring more membrane area to achieve the desired serum protein yield. This required membrane area further has of course consequences for the capital and operational expenditures that are required. The membrane area together with the performance based on the purity and retentate and permeate recoveries shapes any decision on the membrane configuration to choose.

5. Conclusion

The effectiveness of skim milk fractionation using concentration and diafiltration is affected by the membrane module configuration, membrane area as well as by the operating conditions. During the initial concentration step, the resulting flux is lower for spiral wound membranes than for hollow fiber membranes. Evaluation of the mass fluxes clearly shows that hollow fiber membrane achieves more serum protein per m^2 surface area and hour of operation. During diafiltration, the serum mass flux for hollow fiber membranes is again higher than that of spiral wound membranes. This is reflected in the serum protein yield as hollow fiber membranes yield is 1.2 to 1.5 times higher as compared to

the yield of spiral wound membranes. To compensate for this, a 7 times larger membrane area is needed for spiral wound membranes. Additionally, at equal yield, hollow fiber membranes achieve higher serum protein purity as compared to spiral wound membranes. Based on the experimental results for spiral wound module of 0.3 m and hollow fiber module of 0.75 m, profiles such as flux and yield profiles were developed that can help to identify the balances that need to be sought between yield and purity of the serum proteins, and between the recoveries of both the serum proteins and the loss caseins in the permeate.

CRediT authorship contribution statement

Hilda Lucy Nyambura: Writing – review & editing, Supervision, Conceptualization. **Anja E.M. Janssen:** Writing – review & editing, Supervision, Conceptualization. **Remko M. Boom:** Writing – review & editing, Supervision, Conceptualization. **Albert van der Padt:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.seppur.2025.135544.

Data availability

Data will be made available on request.

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