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# Optimization of Solute Separation by Diafiltration

Paul Ng[a]; John Lundblad[a]; Gautam Mitra[a]
[a] Biochemical Development Cutter Laboratories, Inc., Berkeley, California

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# NOTE

## Optimization of Solute Separation by Diafiltration

PAUL NG, JOHN LUNDBLAD, and GAUTAM MITRA

BIOCHEMICAL DEVELOPMENT
CUTTER LABORATORIES, INC.
BERKELEY, CALIFORNIA 94710



**Abstract**

Preliminary consideration suggests that process time in diafiltration can be optimized. A mathematical derivation of the optimum time gives a surprisingly simple general relationship between the bulk concentration and the membrane surface concentration. Experimental values confirm that an optimum value can indeed be obtained.

Up to now, most plasma processors rely on lyphilization as the classical approach for the separation of ethanol from plasma proteins. Friedli and Kistler (*1*) and Dickson and Smith (*2*) have suggested that gel filtration is a practical alternative to lyphilization. Certain drawbacks such as small charge volume and inhibition of bacterial growth limit its applications.

We have evaluated diafiltration as a means of removing salt and alcohol. Experiments with an Amicon Thin-Channel TCF-10 System confirm that solute separation from plasma proteins falls exponentially with time following a first-order decay curve. Total time for diafiltration is determined by the ultrafiltrate flux and the total desired volume change. For the same amount of protein, the bulk concentration can be manipulated by adding an appropriate amount of buffer. While the use of low concentration is attractive in terms of higher flux, it must be counterbalanced by the

increase in permeate volume. Preliminary consideration suggested that an optimum concentration could be obtained to give a minimum amount of process time.

The film theory for mass transfer relates the local ultrafiltrate flux, J, to concentration of solute by the following relationship (*3*):

$$J = k \ln \frac{C_w - C_p}{C_b - C_p} \tag{1}$$

where $k$ = local mass transfer coefficient for protein between the bulk solution and the membrane surface
$C_w$ = concentration at the wall
$C_p$ = concentration in the permeate
$C_b$ = concentration in the bulk solution

For high membrane rejection, $C_w \gg C_p$, Eq. (1) becomes

$$J = k \ln \frac{C_w}{RC_b} \tag{2}$$

where $R$ = rejection coefficient defined by $1 - (C_p/C_b)$

For a fixed amount of protein $P$, the total volume of permeate $V$ is related to the number of changes, $n$, by

$$V = nP/C_b \tag{3}$$

Process time per unit area is

$$t = V/J$$

or

$$t = \frac{nP/C_b}{k \ln C_w/RC_b} \tag{4}$$

In order to optimize Eq. (4), the following assumptions are made:

(a) Constant $C_w$. Vilker et al. (*4*) have clearly demonstrated that the concentration at the membrane surface is merely the osmotic equivalent of the applied pressure.
(b) Constant $k$. For fully developed flow, $k$ is a function of diffusivity (*3*). Colton et al. (*5*) have demonstrated that Eq. (2) holds for average bulk protein concentration between 1 to 20 g/100 ml. This suggested that a constant diffusivity can be used within these limits.

Differentiating $t$ with respect to $C_b$,

$$\frac{dt}{dC_b} = \frac{-nP}{kC_b^2 \ln (C_w/RC_b)} + \frac{nP}{kC_b^2 \ln (C_w/RC_b)^2} \tag{5}$$

By setting $dt/dC_b = 0$, Eq. (5) becomes

$$1 = \ln C_w/RC_b^*$$

or

$$C_b^* = C_w/Re \tag{6}$$

where $C_b^*$ = optimum bulk protein concentration

Thus one could predict an optimum value if the membrane surface concentration and the rejection coefficient can be precisely measured. Conversely, $C_w$ can be calculated from $C_b^*$. Above 800 molecular weight, a rejection coefficient of 1.0 can be used (*6*, *7*), and Eq. (6) becomes

$$C_b^* = C_w/e \tag{7}$$

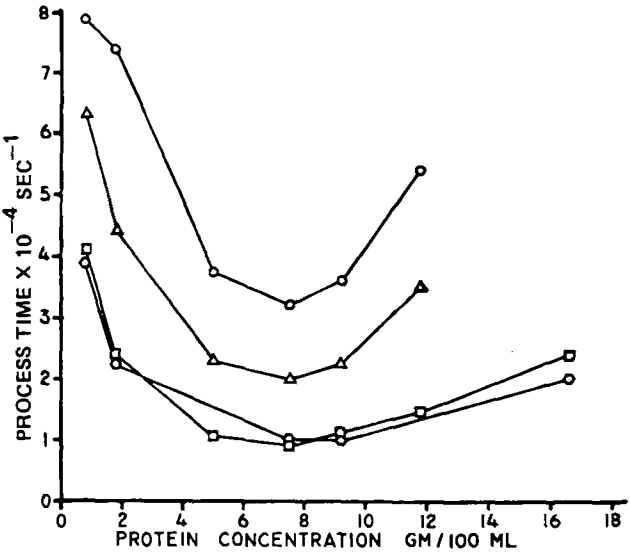


FIG. 1. Human seum albumin. Diafiltration at pH = 6.8, 22°C, and 25 psig. Shear rate per unit length (cm sec)$^{-1}$: (○) 119.9, (△) 225.4, (□) 326.1, (○) 431.6.

Extensive data of ultrafiltrate flux, protein content, and shear rate for albumin solution (M.W. 65,000) have been previously reported (*8*). Figure 1 is a plot of the process time (per unit area and per unit weight of protein) vs the protein concentration. Curves for all four shear rates converge to a minimum process time. This appeared to lie between 7 and 8 g/100 ml of protein concentration. Thus $C_w$ is in the vicinity of 19.11 g/100 ml to 21.84 g/100 ml. This compares with literature values of 20 wt% or greater and 28.7 wt-% predicted by Bixler et al. (*6*) and by Colton et al. (*5*).

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