Korean J. of Chem. Eng., **13**(5), 457-465 (1996)

PREDICTION OF MACROMOLECULAR TRANSPORT THROUGH THE DEFORMABLE POROUS MEDIA OF AN ARTERY WALL BY PORE THEORY

Woo-Sik Kim† and John M. Tarbell*

Department of Chemical Engineering, Institute of Material Science and Technology,
Kyunghee University, Yongin, Keeheung, Seochun 1, Kyungki-Do, Korea
*Department of Chemical Engineering, The Pennsylvania State University, University Park, PA 16802, U.S.A.
(*Received 3 April 1996 • accepted 16 July 1996*)

Abstract – To determine the transport properties of macromolecules in the media of an artery wall deformed inhomogeneously by the transmural pressure, we combine a simple mechano-hydraulic model based on a two parameter strain-dependent permeability function, which was developed by Klanchar and Tarbell [1987], with a pore theory. The combined theory allows us to calculate the spatial distributions of porosity, solute partition, pore radius and macromolecular solute concentration in the media and their dependence on the transmural pressure. The predictions from the pore theory are in good agreement with experimental measurements of sucrose space, albumin space and albumin concentration profiles in the media of rabbit aortas at transmural pressures of 70 and 180 mmHg. The prediction indicates that albumin transport through the aortic media is dominated by convection rather than diffusion. It is further demonstrated that the transport properties of planar tissue samples, which are often used in *in vitro* experimentals, may be quite different from those of intact vessels in their natural cylindrical configuration because of the variation in tissue deformation. Using the pore theory we are also able to calculate the interstitial shear stress associated with transmural volume flow which may act on the smooth muscle cells residing in the media and find it to be on the order of several dyne/cm^2. This level of shear stress will stimulate endothelial cells and may also affect smooth muscle cells.

Key words: *Deformable Media, Pore Theory, Macromolecular Transport, Sucrose Porosity, Albumin Porosity*

INTRODUCTION

Since it is believed that disease of atherosclerosis is due to the abnormal accumulation of macromolecules in the artery wall, many studies on the macromolecular transport through the artery wall has been rigorously performed. Tedgui and Lever [1985, 1987] have carried out the albumin transport through rabbit aorta media. According to their study the albumin concentration in media of damaged artery was higher than that in media of intact artery and the albumin concentrations in both cases were significantly influenced with transmural pressure. Curmi et. al [1990] also showed the important role of transmural pressure on the macromolecular transport in the rabbit aorta media.

To elucidate the mechanism of macromolecular transport through artery wall a number of mathematical models have been developed. Truskey et al. [1981] and Fry [1985] have presented one-dimensional, multilayer models accounting for transport resistances associated with the intima (endothelium, basement matrix, internal elastic lamina), media and advantitia. Yuan et al. [1991] have developed elaborate two-dimensional models which describe intimal transport in great detail; accounting for lateral convection in the sub-intima, molecular sieving through the internal elastic lamina, and leaky endothelial junctions. However, all of these models are based on the rigid, non-deformable structure; yet the artery wall is clearly a deformable elastic structure having internal stresses which depend on the transmural pressure. Indeed, Tedgui and Lever [1984] have observed that hydraulic conductivity of the rabbit thoracic aorta decreases as the transmural pressure increases, presumably due to compaction of the media associated with increased wall stress.

To describe the pressure dependence of hydraulic conductivity observed by Tedgui and Lever [1984], a simple mechano-hydraulic model of the arterial media based on a two parameter strain-dependent permeability function was developed by Klanchar and Tarbell [1987]. By combining this mechano-hydraulic model with a fiber matrix theory [Curry, 1984], Kim and Tarbell [1994] have developed the fiber matrix model to predict the spatial variation and transmural pressure dependence of the medial transport properties (e.g., porosity, pore radius and effective diffusivity).

In the present paper we suggest a pore model which is derived by combination of mechano-hydraulic model with the pore theory. This pore model allow us to predict macromolecular transport across the artery media as well as to calculate the shear stress on pore walls associated with the transmural flow, and we suggest that this provides an estimate of the shear stress imposed on the surface of smooth muscle cells.

MODEL OF FLOW IN DEFORMABLE POROUS MEDIA (CYLINDRICAL GEOMETRY)

The theory to be outlined below applies to the media of an intact artery wall in the cylindrical geometry of Fig. 1. The mechano-hydraulic model was derived from combining Darcy's

†To whom correspondence should be addressed.

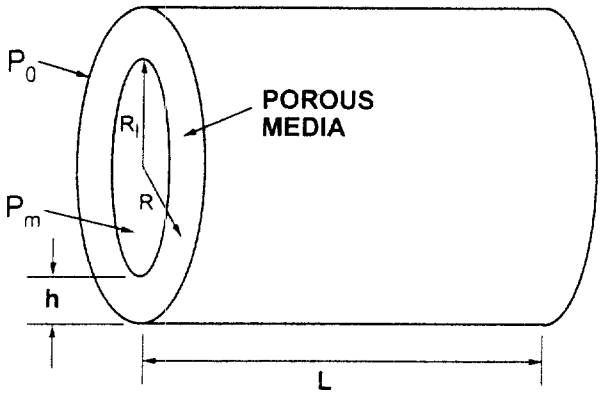

Fig. 1. Cylindrical geometry of the porous media.

law for the transmural flow with force balance on the media for deformation [Klanchar and Tarbell, 1987] and suggested the following expression for the fluid filtration velocity.

$$V_s = \frac{\kappa_0 P_m}{\mu R\left[\frac{h}{R_I}\left(1-\frac{h}{2R_I}\right)-\frac{P_m M}{2(\lambda+G)}\right]} \tag{1}$$

where P_m is the transmural pressure drop across the deformable porous media of thickness h, κ_0 is the permeability of the underformed media, μ is the fluid viscosity, M is a material constant, and λ and G are the Lame constants of the media. Eq. (1) shows that the hydraulic conductivity of the media (V_s/P_m) depends on the transmural pressure difference (P_m). From the mechano-hydraulic model the spatial dependence of the permeability in the media was derived as follows [Klanchar and Tarbell, 1987],

$$\frac{\kappa}{\kappa_o} = \frac{-R^{-a}}{b(a+2)} \tag{2}$$

where a and b are constants determined by the boundary conditions on the inner and outer surfaces of the media which are available in Klanchar and Tarbell [1987] and Kim and Tarbell [1994]. The connection between the phenomenological theory outlined above and the pore theory through the permeability κ will result in the expression for transport parameters in the intact artery media.

1. PORE THEORY

The pore theory suggested by Anderson and Quinn [1973] describes the media as a bundle of straight circular capillary tubes. This theory has been used to predict flow and diffusion through synthetic membranes. A more realistic description of porous media was presented by McKinley et al. [1966] who introduced a tortuosity factor (τ) and a second factor (α), related to the pore size distribution and pore geometry, both of which would affect the local pressure gradient. Using τ and α the parabolic velocity profile in a pore of radius, r_p, is expressed as

$$V(r) = \frac{r_p^2}{4\mu\tau\alpha}\left(1-\frac{r^2}{r_p^2}\right)\left(-\frac{dP}{dR}\right) \tag{3}$$

and the volume flow in a pore, Q_p, is then given by

$$Q_p = 2\pi\int_0^{r_p} V(r)\cdot r\,dr = \frac{\pi r_p^4}{8\mu\tau\alpha}\left(-\frac{dP}{dR}\right) \tag{4}$$

If the total number of pores, N, is independent of the deformation of the media, the superficial velocity, V_s, can be expressed as,

$$V_s \equiv \frac{NQ_p}{2\pi RL} = \frac{\varepsilon r_p^2}{8\mu\tau^2\alpha}\left(-\frac{dP}{dR}\right) \tag{5}$$

where the porosity, ε, is defined by

$$\varepsilon = \frac{N\pi r_p^2\tau}{2\pi RL} \tag{6}$$

and L is the length of the cylindrical arterial segment containing N pores. The shear stress on the wall, τ_{pw}, can be obtained from Eqs. (3) and (5) with the result

$$\tau_{pw} = \frac{4\mu\tau V_s}{r_p\varepsilon} \tag{7}$$

By equating the expression for V_s in Eqs. (1) and (5), we obtain a relationship for the permeability in terms of pore theory parameters,

$$\kappa = \frac{\varepsilon r_p^2}{8\tau^2\alpha} \tag{8a}$$

or

$$r_p = \tau\sqrt{8\alpha\frac{\kappa}{\varepsilon}} \tag{8b}$$

Eq. (8b) is identical with the expression for the pore radius of the media proposed by McKinley et al. [1966]. The tortuosity of the media (τ) is the ratio of the actual length of the flow path to the linear length of the media and is directly related to the structure and porosity of the media. Kim and Tarbell [1994] used the following simple relationship between tortuosity and porosity, which was suggested by Muhr and Blanshard [1982]:

$$\tau = \frac{1}{\varepsilon} \tag{9}$$

The parameter α, which depends on the structure of the media, will be assumed constant (independent of spatial position) and will be used as an adjustable parameter to fit experimental data. Since the spatial variation of κ was determined previously [Eq. (2)], the spatial variation of the porosity and pore radius can now be determined from Eqs. (2), (6), (8) and (9), with the result of

$$\frac{r_p}{r_{po}} = \left(\frac{R}{R_{IO}}\right)^{3/10}\left(\frac{-R^{-a}}{b(a+2)}\right)^{1/5} \tag{10}$$

$$\frac{\varepsilon}{\varepsilon_o} = \left(\frac{r_p}{r_{po}}\right)\left(\frac{R_{IO}}{R}\right)^{1/2} \tag{11}$$

In Eqs. (10) and (11), the subscript zero denoted the unstrained state of the media.

We will also find it useful to have a pore theory expression

for solute porosity, ε_s, for subsequent comparison of the theory with experimental data. As shown by Curry [1984],

$$\varepsilon_s = \Phi\varepsilon \tag{12}$$

where Φ is the partition coefficient, which for a circular pore is given by

$$\Phi=(1-\beta)^2 \tag{13}$$

where $\beta=a_s/r_p$ and a_s is the radius of solute.

The flux equation for a solute in a pore was developed by Anderson and Quinn [1973] for a synthetic membrane as follows,

$$N_s = -k_d D_\infty \frac{dC}{dR} + k_c \overline{V} C \tag{14}$$

where C is concentration of solute in the pore, D_∞ is the diffusivity of the solute in dilute bulk solution and V is the mean fluid velocity in a pore ($\overline{V}=Q_p/\pi r_p^2$) which is related to superficial velocity through the porosity ($V_s=\varepsilon\overline{V}$). k_c and k_d are the integrated lag and inverse drag coefficient, respectively, which were defined by Anderson and Quinn [1973] using the equation of motion of a spherical particles in a cylindrical tube and evaluated by Deen [1987] with a center line approximation as,

$$k_d = \frac{2}{\Phi}\int_0^{1-\beta} K^{-1}\gamma d\gamma = K^{-1} \tag{15}$$

$$k_c \equiv \frac{4}{\Phi}\int_0^{1-\beta} G(1-\gamma^2)\gamma d\gamma = (2-\Phi)G \tag{16}$$

In Eqs. (15) and (16), γ is defined as r/r_p and K and G are drag and lag coefficients, respectively, which have been provided by Happel and Brenner [1986] as follows:

$$K^{-1} = 1-2.10444\beta+2.08877\beta^3-0.94813\beta^5-1.372\beta^6 +3.87\beta^8-4.19\beta^{10} \tag{17}$$

$$G = \frac{1-2}{3}\beta-0.1628\beta^3-0.4059\beta^7+0.5236\beta^9+1.51\beta^{10}+\cdots \tag{18}$$

Eqs. (17) and (18) are in good agreement with the exact theory of Haberman [Happel and Brenner, 1986] for $0<\beta<0.6$, but for higher values of β there may be significant deviations. As we shall see, in fitting arterial wall mass transport data for albumin we will encounter $\beta>0.6$, and in such a case interpolation of Harberman's exact values for K^{-1} and G will be employed.

At steady state the mass balance for solute in the media is expressed as,

$$\frac{dN\pi r_p^2 N_s}{dR} = 0 \tag{19}$$

Inserting Eqs. (6) and (14) into Eq. (19) we arrive at

$$\frac{d}{dR}R\varepsilon\frac{D_\infty k_d}{\tau}\frac{dC}{dR} - \frac{d}{dR}Rk_c V_s C = 0 \tag{20}$$

The term $D_\infty k_d/\tau$ corresponds to the effective diffusivity of the porous media derived by Truskey et al. [1981]. Based on the form of Eq. (20), a dimensionless Peclet number, indicative of the relative roles of convection to diffusion in the overall transport process, can be defined as follows:

$$N_{Pe} = \frac{k_c V_s h}{\varepsilon D_\infty k_d/\tau} \tag{21}$$

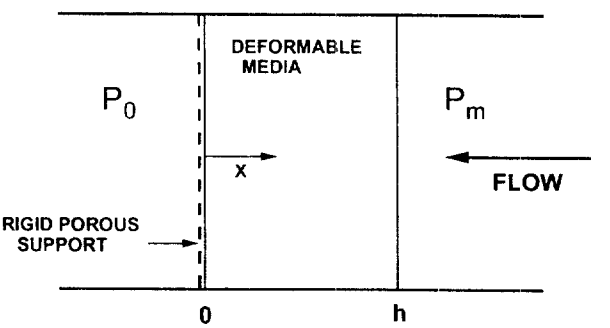

Fig. 2. Planar geometry of the porous media.

Using the equation for spatial variation of the transport properties obtained previously, Eq. (20) can be solved numerically to obtain the solute concentration profile in the porous media even if it is deformed inhomogeneously.

MODEL OF FLOW IN DEFORMABLE POROUS MEDIA (PLANAR GEOMETRY)

Transport experiments are often conducted with excised arterial tissue samples that have been cut lengthwise and mounted flat against a rigid porous support as shown schematically in Fig. 2 [Bratzler, 1974; Harrison and Massaro, 1976]. The transport theory developed in the preceding section for the cylindrical geometry will be outlined below for the planar case. As we shall see, there are significant differences in the transport properties of the tissue in these two configurations.

Applying Darcy's law, force balance and strain dependent permeability function for the planar geometry, the superficial velocity and permeability of the media are easily calculated [Klancher and Tarbell, 1987],

$$V_s = \kappa_0(\lambda+2G)\ln\frac{\left[\frac{1-P_m M}{(\lambda+2G)}\right]}{\mu M h} \tag{22}$$

$$\frac{\kappa}{\kappa_0} = \left(-\frac{P_m M}{(\lambda+2G)}\right)^{(x/h-1)} \tag{23}$$

Combining Eq. (23) with pore theory will give the expression for the spatial dependence of the transport properties in the media.

1. Pore Theory

The pore theory is independent of the overall tissue geometry and remains that defined by Eqs. (5)-(9) with R replaced by x. Making the same assumptions as outlined previously and combining the pore theory equation with Eq. (23), we obtain the spatial dependence of the pore radius and porosity in the media as follows:

$$\frac{r_p}{r_{po}} = \left(1-\frac{P_m M}{(\lambda+2G)}\right)^{1/5(x/h-1)} \tag{24}$$

$$\frac{\varepsilon}{\varepsilon_0} = \frac{r_p}{r_{po}} \tag{25}$$

The mass balance for the solute in the media takes a form analogous to Eq. (20) for the cylindrical geometry,

$$\frac{d}{dx}\varepsilon\frac{D_\infty k_d}{\tau}\frac{dC}{dx} - \frac{d}{dX}\kappa_c V_s C = 0 \tag{26}$$

The previously developed expression for the lag and drag coefficients [Eqs. (17) and (18), respectively] are also used for the planar media.

COMPARISON WITH EXPERIMENTAL DATA

1. Cylindrical Geometry

The only comprehensive set of data available for evaluation of arterial wall transport theories was obtained by the group at Imperial College, London. Tedgui and Lever [1984] measured filtration velocity (V_s) in cylindrically mounted intact rabbit thoracic aortas at 70 and 180 mmHg. Caro et al. [1981] measured sucrose space (ε) and albumin space (ε_s) in the media of intact rabbit thoracic aortas at 0, 70 and 180 mmHg, and Tedgui and Lever [1985] determined the concentration distribution of albumin in the same vessels and at the same pressures.

In Eq. (3) the deformation parameters κ_0/μ and for intact rabbit aorta are evaluated by Kim and Tarbell [1994] with experimental data of Tedgui and Lever [1984] and Baldwin et al. [1992]. These evaluated parameter values provide the best fit to the hydraulic conductivity with the experimental data.

The adjustable parameters of the pore theory (ε_o and α) are determined by fitting the ε and ε_s data of Tedgui and Lever [1987]. It should be noted that Tedgui and Lever [1987] provide spatially averaged values of ε and ε_s across the media of the intact aorta. Thus, we integrate the spatial distributions of ε and ε_s over the media to obtain spatially averaged values for comparison with the data. In the performing these calculations, we have used the data of Tegui and Lever [1984] to determine pressure drop across the endothelial layer which is required for calculation of the superficial velocity Eq. (3). The theoretical predictions and data are compared in Fig. 3 where it is apparent that the pore theory is in accord with the data over a broad range of transmural pressures. The adjustable parameters are ε_0=0.43 and α=0.97.

The albumin transport experiments of Tedgui and Lever [1985] were conducted so that the diffusive flux was directed from outside of the wall to lumen while the convective flux, driven by the transmural pressure gradient, was in the opposite direction. In the experiments the distribution of relative albumin concentration (C_t/C_b), that is the ratio of albumin concentration in the medial tissue (C_t) to that in the bulk solution (C_b), was measured at 70 and 180 mmHg. For comparison of our predictions with the data, the solution of governing equation [Eq. (20)] giving the interstitial albumin concentration (C) is converted to the relative concentration $\varepsilon C/C_b$. The predictions of relative albumin concentration distribution are compared to the data in Fig. 4. The predictions are based on the assignment of boundary values of the relative concentration at $(R - R_i)/h$=0 and 1. The adjustable parameters were set at the same values

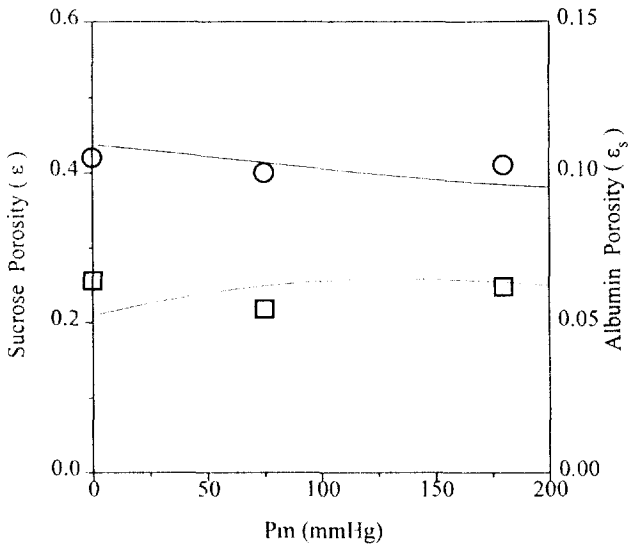

Fig. 3. Comparison between the predictions and experimental data [Tedgui and Lever, 1987] for sucrose porosity (ε) and albumin porosity (ε_s) in the rabbit aortic media. Curves 1 and 2 are predictions of pore theory for ε and ε_s, respectively, with ε_o=0.43 and α=0.97 Å. ○ and □ -experimental data for ε and ε_s, respectively.

required to fit and data (Fig. 3) and no other parameters were adjusted. It is apparent from the shapes of the concentration profiles that convection is the dominant transport mechanism at both 70 and 180 mmHg. The pore theory is in excellent agreement with data at 70 mmHg, but predicts too great a role for convection at 180 mmHg. It should be noted that the prediction of albumin transport in the intact aorta media by the fiber matrix theory is in good agreement with the data at 180 mmHg but underestimates the relative importance of convection at 70 mmHg [Kim and Tarbell, 1994].

Actually, since the artery media is composed of various kinds of muscle fibers and elastins and has a complex internal structure, it may be not proper to simply assume that the deformation modulus and elastic properties in the media may be homogeneous. Thus, the deformation of media under the transmural pressure could not be exactly described by the simple mechano-hydraulic model and it may result in the deviation of pore model prediction of albumin concentration profile from the experimental data.

The relative importance of convection predicted by the pore theory is reflected in the computed Peclet numbers. The pore theory predicts Peclet numbers of 5.65 and 17.12 at 70 and 180 mmHg, respectively while, according to Kim and Tarbell [1994], the fiber matrix theory predicts Peclet numbers of 3.50 and 7.70 at the same transmural pressures. Tedgui and Lever [1985] predicted Pe=4.12 at 70 mmHg and Pe=4.65 at 180 mmHg by curve fitting their experimental data to the convective-diffusion equation of a non-deformable material. The pore theory predicts the magnitude of the Peclet number reasonably well, but it overpredicts the sensitivity to transmural pressure.

2. Transport Properties Based on Pore Theory

Using characteristic parameters of the rabbit thoracic aorta as described above we have calculated the spatial dependence of

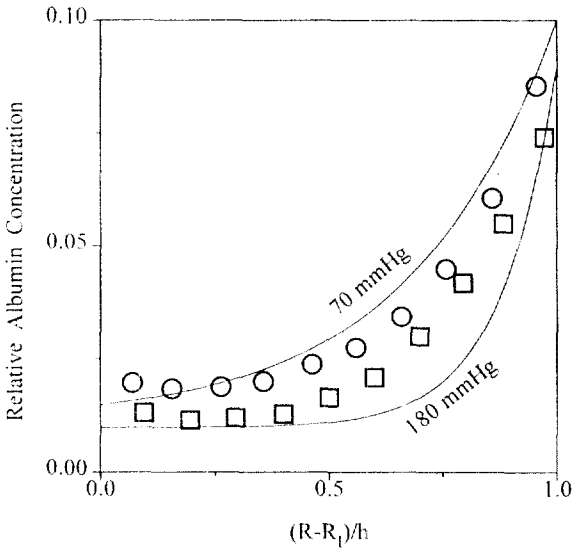

Fig. 4. Comparison between the predictions and experimental data [Tedgui and Lever, 1985] for albumin concentration distributions in the rabbit aortic media. predictions with adjustable parameters of ε_o=0.43 and α=0.97 Å. ○ - experimental data at 70 mmHg and □ -at 180 mmHg.

porosities (ε and ε_s) and the pore radius (r_p) as displayed in Figs. 5 and 6. These properties are all very weakly dependent upon position. ε and ε_s are moderately dependent on the transmural pressure, but r_p is relatively insensitive, varing by only 10% as pressure is varied between 180 mmHg and 70 mmHg. The effective diffusivity for albumin ($D_\infty k_d/\tau$) is also insensitive to position having a value of 1.7×10^{-12} m^2/s at 70 mmHg and 0.84×10^{-12} m^2/s at 180 mmHg. These values are in close accord with estimates for rabbit thoracic aortas *in vivo* (1.1×10^{-12} m^2/s) presented by Truskey et al. [1981] obtained by fitting the convective-diffusion equation to albumin concentration profiles. These diffusivity values are of course much lower than the value for albumin in aqueous solution 6.8×10^{-11} m^2/s [Truskey et al., 1981].

From the pore theory model the shear stress on the media wall can be predicted. The theory shows that the pore wall shear stress is also insensitive to spatial position, but varies from 0.1 N/m^2 at 70 mmHg to 0.3 N/m^2 at 180 mmHg.

It must be emphasized that the transport properties, although dependent on the transmural pressure, are predicted to be insensitive to spatial position within the media in the cylindrical geometry. This is consistent with observations of Truskey et al. [1981], Tedgui and Lever [1984] and others, that medial concentration profiles are fit very well by classical convective-diffusion theory with constant effective transport properties. As we shall see, this is not the case for transport in the planar geometry of Fig. 2.

3. Planar Geometry

Even though the planar geometry is often used for *in vitro* measurement of transport in the artery wall, a comprehensive set of experimental data giving the porosity and solute transport within the arterial media in the planar geometry has not yet been reported. Thus, for prediction of transport properties in planar media, the same parameter values obtained previously

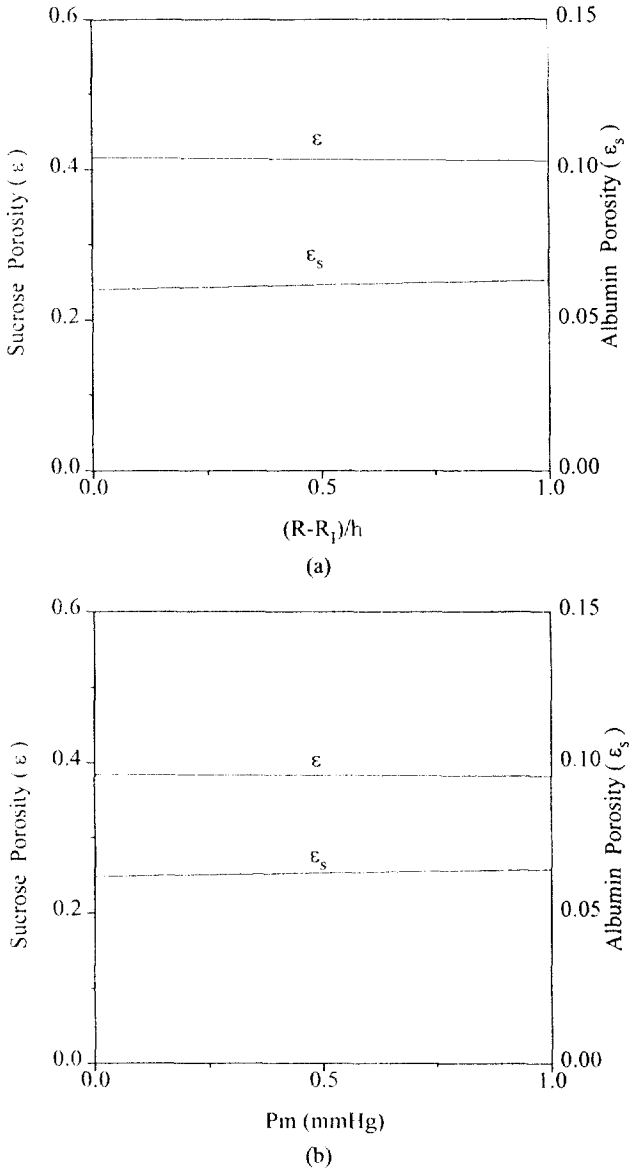

Fig. 5. Porosity distributions in the cylindrical aortic media predicted by the pore theory.
— sucrose porosity (ε) and --- albumin porosity (ε_s). a: 70 mmHg, b: 180 mmHg.

for the intact cylindrical rabbit aorta are employed. In permeability studies of Klanchar and Tarbell [1987] and Kim and Tarbell [1994] the modulus of the media ($H_A=\lambda+G$) was reduced to reflect the fact that tissue become more deformable after reduction of hoop stress in the relaxed planar geometry. Klanchar and Tarbell [1987] suggest a value of $H_A/471$ and Kim and Tarbell guess the value of $H_A/2300$ to actually provide the best fit to water flux data available in the planar geometry [Bratzler, 1974]. Thus, we consider the same reductions of the media modulus to predict the albumin concentration distribution and transport properties in the planar media.

4. Transport Properties Based on the Pore Theory

In Fig. 7 the prediction of the pore radius is displayed as function of spatial position in the media at the transmural pressure differences of 70 and 180 mmHg. The spatial distribution

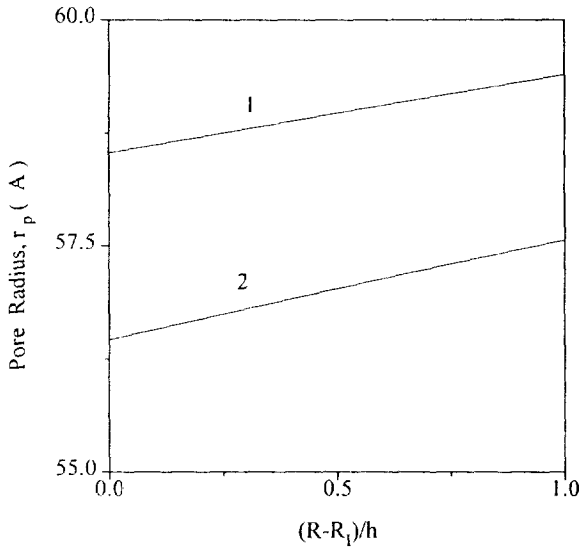

Fig. 6. Pore radius distribution in the cylindrical aortic media used to predict the transport properties in the media.
1: 70 mmHg, 2: 180 mmHg.

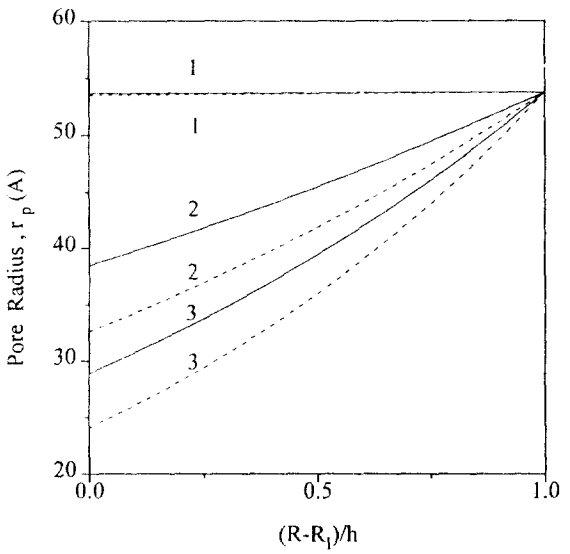

Fig. 7. Pore radius distribution in the planar at 70 mmHg (—) and 180 mmHg (---).
1: Reduction factor=1.0, 2: Reduction factor=471, 3: Reduction factor=2300.

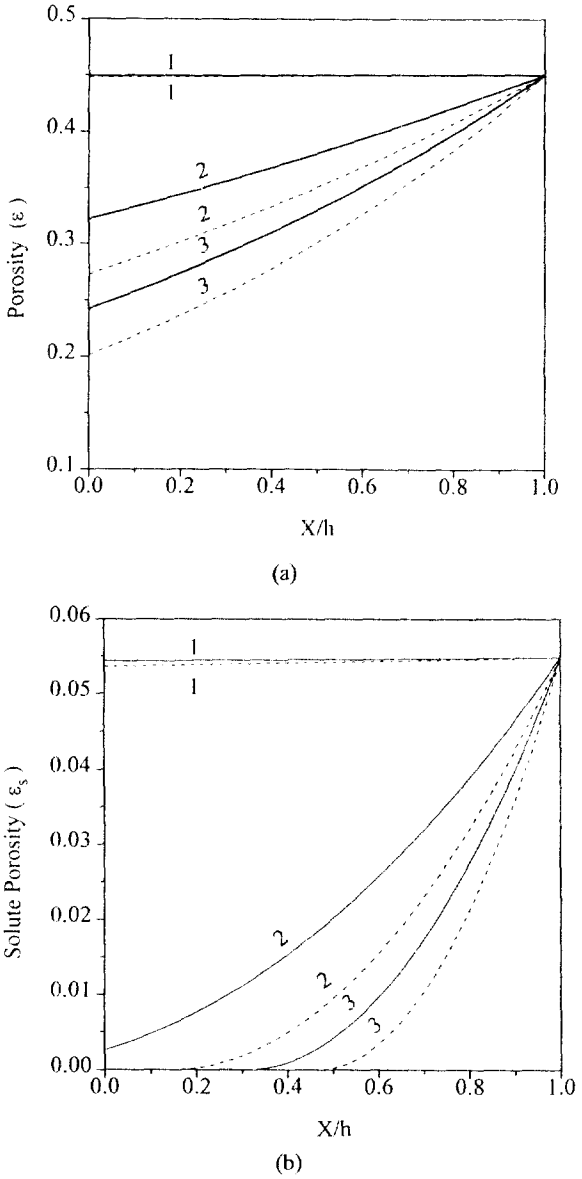

Fig. 8. Porosity distributions in the planar media predicted by the pore theory at 70 mmHg (—) and 180 mmHg (---).
1: Reduction factor=1.0, 2: Reduction factor=471.0 and 3: Reduction factor=2300.0. (a) Sucrose Porosity and (b) Albumin Porosity.

of pore radius is greatly affected by reduction of the modulus of the media. The pore radius is insensitive to spatial position in the stiff material (reduction factor of 1.0), but becomes increasingly more sensitive to position as the material becomes more deformable (reduction factor increases). At a reduction factor of 2300, the result reveals that the pore radius becomes smaller than the radius of albumin (a_s=35Å) over a region of the media of the media near the grid, and zero solute porosity is predicted as shown in Fig. 8.

The distribution of pore wall shear stress is displayed in Fig. 9, and it is also expected to become more sensitive to position with the reduction of the modulus. The pore wall shear stress in the planar media is predicted to have a similar value in the cylindrical geometry for the same value of the media modulus and transmural pressure differential.

In Fig. 10, the predicted relative albumin concentration distribution in the media is displayed for two different cases in which the bulk concentrations (C_b) of the bathing solutions on upstream (x/h=1) and downstream (x/h=0) sides of the porous media have been specified. In one the convective transport of albumin is in the opposite direction of the diffusive transport (C_b=1.0 at x/h=0 and C_b=0.05 at x/h=1) and in the other case both transport mechanisms are in the same direction (C_b=0.05 at x/h=0 and C_b=1.0 at x/h=1). For both cases of the boundary conditions, convective transport dominates diffusive transport, and this trend becomes more dramatic with the reduction of the modulus of the media (c.f, Fig. 10). Consequently, these pre-

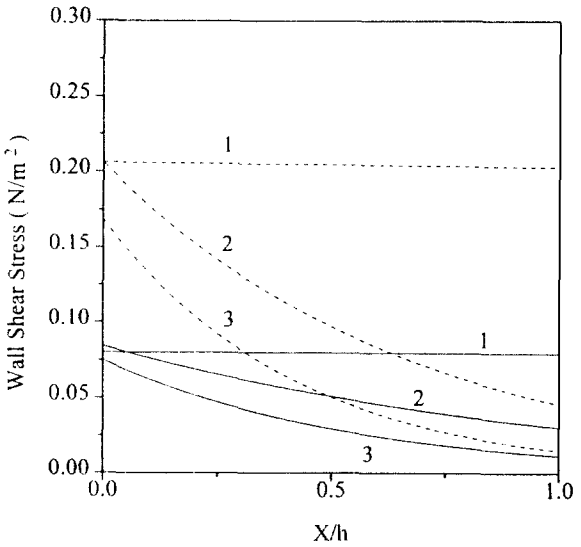

Fig. 9. Wall shear stress distributions in the planar media predicted by the pore theory.
— 70 mmHg and --- 180 mmHg.

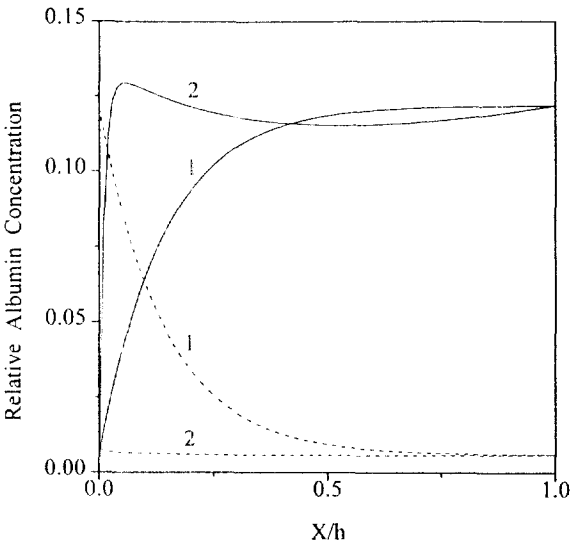

Fig. 10. Albumin concentration distributions in the planar media predicted by the pore theory.
--- boundary condition set for diffusive flux opposite to convective flux; — boundary condition set for diffusive and convective fluxes in the same direction.

dictions of the pore theory in planar geometry of the media imply that the concentration distribution is highly dependent on tissue stiffness and the dominant contribution to the overall transport is shifted from the convective to diffusive transport as the tissue becomes softer.

DISCUSSION

In this study a mathematical model to predict the variation of transport properties in deformable porous media resulting from changes in the transmural pressure was developed by using the pore theory. The pore theory required the determination of two adjustable parameters from the comparison of model predictions with experimental data. Predictions by the pore theory showed good agreement with limited experimental data for the porosity and albumin partition and fair agreement for the albumin concentration distribution in rabbit aortic media.

Since the pore model describes the media as a bundle of capillary tubes having a single pore size, this model is limited in its ability to predict the transport of solutes over a wide range of molecular size. To overcome the shortage of the pore model the multiple discrete pore sizes or a continuous distribution of pore sizes following some reasonable distribution can be considered. However, these approaches have not been considered here, but would be worth investigating if a more extensive data base were available to allow discrimination among various models.

One advantage of the pore theory is that it provides a means of estimating the shear stress imposed by transmural flow on the surfaces of the solid components of the media by means of the pore wall shear stress. The magnitude of the predicted pore wall shear stress in the rabbit aortic media (0.1-0.3 N/m^2) is in the range which is known to affect endothelial cells *in vitro* [Jo et al., 1991]. At present, the sensitivity of smooth muscle cells which reside in the media to shear stress is not known quantitatively. However, it has been shown that smooth muscle cells in culture will respond to shear stress (cell washing), displaying rapid and significant increase in cytosolic free calcium and sodium [Garay et al., 1989]. If the calculated pore wall shear stress is to act fully on the surface of smooth muscle cells, then it is implicit that the flow is predominantly around the cells and not through them. Whether or not this is the case is not known directly at the present time. However, it is believed that more than 90% of the transmural flow passes around and not through endothelial cells [Renkin and Curry, 1979]. This situation may be similar for similar muscle cells.

According to the pore model we have developed, in the cylindrical arterial configuration under conditions of normal or elevated transmural pressure, the medial tissue of the rabbit aorta is quite stiff and resists compaction by the transmural flow. The result is that the properties of tissue (porosities and diffusivity) do not vary significantly with the position across the media, although they are sensitive to the transmural pressure.

The model makes the interesting prediction that when the axial and hoop stresses on the media are relaxed, as in the planar experiments with excised tissue, and the tissue becomes softer (more deformable), significant compaction of the media can occur. This results in large spatial variations of the tissue properties, and some marked differences in the predictions of albumin concentration distributions between the pore theory (present study) and the fiber matrix theory [Kim and Tarbell, 1994]. Unfortunately, experimental data are not currently available which allow us to judge the accuracy of these predictions.

ACKNOWLEDGEMENT

This work was supported in part by NIH Grant R01-HL 35549.

NOMENCLATURE

a_s : radius of solute
C : concentration of solute per unit void space in the media (interstitial solute concentration)
C_t : tissue concentration
C_b : bulk concentration •
D_{eff} : effective diffusivity
D_∞ : free diffusivity of solute
h : thickness of the media
k : Kozeny constant
k_c : lag coefficient
k_d : drag coefficient
M : material constant
P_m : transmural pressure
R_f : inside radius of the cylindrical media
V_s : fluid filtration velocity

Greek Letters

ε : porosity of media
ε_s : solute porosity of the media
ϕ : partition coefficient
κ : permeability of the media
μ : viscosity of fluid
Ψ : dilation of the media
τ : tortuosity of the media

Subscript

0 : indicates the unstrained state

REFERENCES

Anderson, J. L. and Quinn, J. A., "Restricted Transport in Small Pores: A Model for Steric Exclusion and Hindered Particle Motion", *Biophy. J.*, **14**, 130 (1974).

Baldwin, A. L., Wilson, L. M. and Simon, B. R., "Effect of Pressure on Aortic Hydraulic Conductance", *Atherosclerosis and Thrombosis*, **12**(2), 163 (1992).

Bratzler, R. L., "The Transport Properties of Arterial Tissue", Ph. D. Thesis, Massachusetts Institute of Technology (1974).

Caro, C. G., Lever, M. J. and Tedgui, A., "The Distribution Volumes of Albumin and Sucrose in Arteries Subjected to Normal Mechanical Stresses", *J. Physiol.*, 38P (1981).

Curmi, P. A., Juan, L. and Tedgui, A., "Effect of Transmural Pressures on Low Density Lipoprotein and Albumin Transport and Distribution Across the Intact Artery Wall", *Circulation Research*, **66**(6), 1692 (1990).

Curry, F. E., "Determinants of Capillary Permeability: A Review of Mechanism Based on Single Capillary Studies in the Frog", *Circulation Research*, **59**(4), 367 (1986).

Curry, F. E., "Mechanics of Thermodynamics of Transcapillary Exchange", Handbook of Physiology, Section 2, the Cardiovascular System, Vol. IV, Microcirculation, American Physiology Society, 309, Bethesda, MD (1984).

Curry, F. E. and Michel, C. C., "A Fiber Matrix Model of Capillary Permeability", *Microvascular Research*, **20**, 96 (1980).

Deen, W. M., "Hindered Transport of Large Molecules in Liquid Filled Pores", *AIChE J.*, **9**, 1409 (1987).

Fry, D. L., "Steady-State Macromolecular Transport Across a Multilayered Artery Wall", *Mathematical Modelling*, **6**, 353 (1985).

Garay, R., Rossella, R. and Rosati, C., "Non-Laminar Flow as Initiating Factor of Atherosclerosis: Evidence for a Role of Membrane Ion Transport", in Membrane Technology (Ed. Verna, R.), Raven Press, New York, pp. 137-139 (1989).

Happel, J. and Brenner, H., "Low Reynolds Number Hydrodynamics", Martinus Nijhoff Publishers, Dordrecht, Netherland (1986).

Harrison, R. G. and Massaro, T. A., "Water Flux through Porcine Aortic Tissue Due to a Hydrostatic Pressure Gradient", *Atherosclerosis*, **24**, 363 (1976).

Jo, H., Dull, R. O., Hollis, T. M. and Tarbell, J. M., "Endothelial Albumin Permeability is Shear Dependent, Time Dependent, and Reversible", *Am. J. Physiol.*, **260**, H1992 (1991).

Kim, W.-S. and Tarbell, J. M., "Macromolecular Transport though the Deformable Porous Media of an Artery Wall", *J. of Biomech. Eng.*, **16**, 156 (1994).

Klanchar, M. and Tarbell, J. M., "Modeling Water Flow through Arterial Tissue", *Bull. of Math. Biology*, **49**(6), 651 (1987).

Lai, W. M. and Mow, V. C., "Drag Induced Compression of Articular Cartilage During a Permeation Experiment", *Biorheology*, **17**, 111 (1980).

Lodge, T. P. and Markland, P., "Translational Diffusion of 12-Arm Star Polystyrenes in Dilute and Concentrated Poly (Vinyl Methyl Ether) Solutions", *Polymer*, **28**, 1377 (1987).

McKinley, R. M., Jahns, H. O., Harris, W. W. and Greenkorn, R. A., "Non-Newtonian Flow in Porous Media", *AIChE J.*, **12**(1), 17 (1966).

Muhr, A. H. and Blanshard, J. M. V., "Diffusion in Gels", *Polymer*, **23**, 1012 (1982).

Ogston, A. G., Preston, B. N. and Wells, J. D., "On the Transport of Compact Particles Through Solutions of Chain-Polymers", *Proc. R. Soc. Lond. A*, **333**, 297 (1973).

Patel, D. J. and Varishnay, R. N., "Basic Hemodynamics and Its Role in Disease Processes", University Park Press, Baltimore, MD, 183 (1980).

Phillies, G. D. J., Gong, J., Li, L., Rau, A., Zhang, K., Yu, L. P. and Rollings, J., "Macroparticle Diffusion in Dextran Solutions", *J. of Phy. Chem.*, **93**(16), 6219 (1989).

Renkin, E. M. and Curry, F. E., "Transport of Water and Solutes Across Capillary Endothelium", in Membrane Transport in Biology (Eds., Giebisch, G., Toteson, D. C. and Ussing, H. H.) Springer-Verlag, Berlin, Chapter 1 (1979).

Tedgui, A. and Lever, M. J., "Filtration through Damaged and Undamaged Rabbit Thoractic Aorta", *Am. J. of Physiol.*, **247**, H784 (1984).

Tedgui, A. and Lever, M. J., "The Interaction of Convection and Diffusion in the Transport of ^{131}I-Albumin within the Media of the Rabbit Thoracic Aorta", *Circulation Research*, **57**(6), 856 (1985).

Tedgui, A. and Lever, M. J., "Effect of Pressure and Intimal Damage on ^{131}I-Albumin and [^{14}C] Sucrose Space in Aorta", *Am. J. of Physiol.*, **250**, H1530 (1987).

Truskey, G. A., Colton, C. K. and Smith, K. A., "Quantitative Analysis of Protein Transport in the Arterial Wall", Struc-

ture and Function of the Circulation, Vol. 3, edited by Schwartz, C. J., Werthessen, J. T. and Wolf, S., Plenum Publishing Corporation, New York, NY, 287 (1981).

Yuan, F., Chien, S. and Weinbaum, S., "A New View of Convective-Diffusive Transport Processes in the Arterial Intima", *J. Biomech. Eng.*, in press (1991).