International Journal of Engineering and Applied Sciences (IJEAS)
Vol.2, Issue 3(2010)53-62

MASS TRANSPORT IN ARTERIES AND THE LOCALIZATION OF ATHEROSCLEROSIS IN HUMAN

B. Gutti*[+], *A. A. Susu*[+] *and O. A. Fasanmade*
[+]Department of Chemical Engineering, University of Lagos, Lagos, Nigeria.
and *College of Medicine, University of Lagos, Lagos, Nigeria.

Accepted Date: 14 March 2010

Abstract

Atherosclerosis is a disease of the large arteries that involves a characteristic accumulation of high-molecular weight lipoprotein in the arterial wall. This research focuses on the mass transport processes that mediate the focal accumulation of lipid in arteries and places particular emphasis on the role of fluid mechanical forces in modulating mass transport phenomena as well as analysis of the Damkholer numbers within the arterial surfaces. Blood phase controlled hypoxia was considered in the mass transport mechanisms emerge in the localization of atherosclerosis. The results of the analysis of Damkholer numbers indicated that there were no significant difference between the model derived values of the Damkholer numbers and the corresponding simulated values. Model values ($D_{ar} = 17.7$ *for ATP,* $D_{ac} = 0.02 - 1.0$ *for LDL,* $0.027 - 0.10$ *for albumin,* $D_{aw} = 10.8 - 49.0$ *for oxygen) and simulated value (* $D_{ar} = 7.762$ *for oxygen,* $D_{ac} = 1.214$ *for LDL,* $D_{aw} = 14.58$ *for oxygen); where* D_{ar} *is Damkholer number,* D_{ac} *is Damkholer number based on endothelial permeability and* D_{aw} *is Damkholer number based on the wall consumption. The flux of LDL into the arterial wall depends on the plasma concentration and permeability* P_e *which for human aorta, is between the range of* $5 \times 10^{-4} - 2.5 \times 10^{-3} m/s$. *Thus, a correlation between* P_e *and plasma concentration enhances the localization of atherosclerotic plaques.*

Keywords: Transport, Artheroclerosis, Arteries, Accumulation, Lipoprotein.

1. Introduction

Atherosclerosis is a disease of the coronary, carotid, and other proximal arteries that involves a distinctive accumulation of low-density lipoprotein (LDL) and other lipid-bearing materials in the arterial wall. Atherosclerosis is the leading cause of morbidity and mortality in Western societies. It is a progressive disease characterized by localized plagues that form within the artery wall. As the disease progresses, this plagues enlarge and either directly or indirectly lead to impairment of blood flow [1]. In the advanced stages of atherosclerosis, various complications may occur. One of the most serious of these complications occurs when a blood clot forms in the narrowed artery. Unless the clot is dissolved or is removed through surgery, it may cut off the flow of blood to the tissue normally supplied by the artery, resulting in the death of the affected tissue. This kind of complication often occurs in the major arteries that carry blood to the brain and to the extremities. The disease tends to be localized in regions of curvature and branching in arteries where fluid shear stress (shear rate) and other fluid mechanical characteristics deviate from their normal spatial and temporal distribution patterns in straight vessels. Because of the association of disease with regions of altered fluid mechanics, the role of blood flow in the

localization of atherosclerosis has been debated for many years. Among the first mechanics proposed to relate blood flow to the localization of atherosclerosis was one in which the fluid (blood)-phase resistance to transport of low-density lipoprotein (LDL) or other atherogens was controlled by the local wall shear rate. Studies by Caro and Nerem [2], however, suggested that the uptake of lipids in arteries could not be correlated with fluid-phase mass transport rates, leading to the conclusion that the wall (endothelium) and not the blood was the limiting resistance to transport. This implied that fluid-flow effects on macromolecular transport were mediated by direct mechanical influences on the transport systems of the endothelium. Somewhat later, attention was drawn to the fact that accumulation of macromolecules in the arterial wall depends not on the case by which materials enter the wall, but also on the hindrance to passage of materials out of the wall offered by underlying layers. This brought into focus the possibility that the sub endothelial intima and media layers could be important structures contributing to local macromolecular uptake patterns [3].
This paper determines the mass transport processes that mediate the focal accumulation of lipids in arteries with particular emphasis on the role of fluid (blood) mechanical forces in modulating mass transport phenomena and the localization of atherosclerosis. Model equations of the transport processes to the endothelial cell surfaces in human arteries were developed, and the effect of regions of curvature and branching in arteries, where fluid shear stress and other fluid mechanical characteristics, deviate from their normal spatial and temporal distribution patterns in straight vessels on the localization of atherosclerosis determined. Also the role of fluid (blood) flow in the localization of atherosclerosis was determined.

2. Modeling

Mathematical modeling constitutes a potential technique to contribute and investigate arterial flow dynamics and mass transport. Arterial blood flow dynamics and mass transport phenomena are of great interest in vascular physiology and biology. The main interest concerns the relation between hemodynamic and mass transport and the genesis of diseases (atherosclerosis and thrombosis) in arteries. Modeling helps to gain an insight; where the complete flow field over the vessel space, the shear stress at the fluid endothelium interface and the concentration field of dissolved gases and macro-molecules can be analysed.

2.1. Mathematical Models of Transport to The Endothelial Cell Surface In Human

Here, three common situations for transport that utilized the entire endothelial surface; the reactive surface, the permeable surface, and the reactive wall are modeled to estimate and evaluate the importance of fluid-phase transport relative to other transport processes, kinetics, and mass transfer coefficient [4].

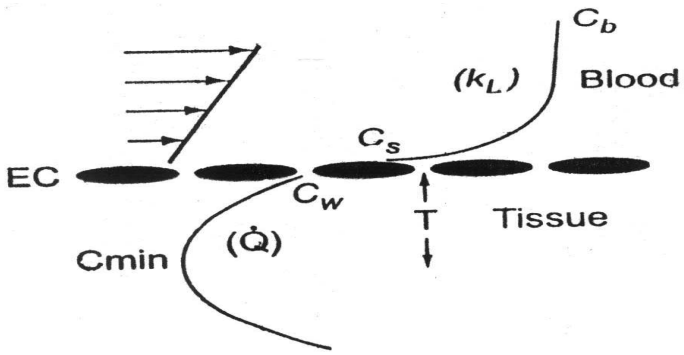

Fig.1. Schematic diagram of arterial wall transport processes.

2.1.1. Reactive Surface

Figure 1 shows a schematic diagram of arterial wall transport processes showing the concentration profile of a solute that is being transported from blood, where its bulk concentration is C_b; to the surface of the endothelium where its concentration is C_s; then across the endothelium, where the sub-endothelial concentration is C_w; and finally to a minimum value within the tissue, $C_{min.}$ It is assumed that the species of interest is transported from the blood vessel lumen, where its bulk concentration is $C_{b,}$ to the blood vessel surface, where its concentration is $C_{s,}$ by a convective-diffusive mechanism that depends on the local fluid mechanism and can be characterized by a fluid-phase mass transfer coefficient K_L. The species flux (mass flow rate divided by surface area) in the blood phase is given by

$$J_s = K_l(C_b - C_s) \tag{1}$$

At the endothelial surface where the species undergo enzyme catalyzed surface reaction, can be modeled using Michaelis-Menten kinetics, with a rate;

$$V = \frac{V_{\max} C_s}{K_m + C_s} \tag{2}$$

When $C_s << K_m$ as is often the case, the reaction rate is pseudo-first order.

$$V = K_r C_s \tag{3}$$

The rate constant for the reaction is given by

$$K_r = \frac{V_{\max}}{K_m} \tag{4}$$

At steady state the transport to the surface is balanced by the assumption at the surface so that

$$K_l(C_b - C_s) = K_r C_s \quad (5)$$

To cast equation (5) into a dimensionless form by multiplying by d/D, then:

$$Sh(C_b - C_s) = D_{ar} C_s \quad (6)$$

and

$$Sh = \frac{K_l d}{D} \quad (7)$$

$$D_{ar} = \frac{K_r d}{D} \quad (8)$$

Solving equation (6) for surface concentration one finds

$$\frac{C_s}{C_b} = \frac{1}{1 + D_{ar}/Sh} \quad (9)$$

When $D_{ar} << Sh$,

$$C_s = C_b \quad (10)$$

And the process is termed “Wall-limited” or “reaction-limited”. On the other hand, when $D_{ar} >> Sh$,

$$C_s = \frac{Sh}{D_{ar}} C_b \quad (11)$$

2.1.2 . Permeable Surface

Many species will permeate the endothelial without reacting at the luminal surface (e.g., albumin, LDL) and their rate of transport (flux) across the surface layer can be described by

$$J_s = P_e(C_s - C_w) \quad (12)$$

If the resistance to transport offered by endothelium is significant,

$$C_s << C_b \quad (13)$$

So that at steady state when the fluid and surface fluxes balance,

$$K_l (C_b - C_s) = P_e C_s \quad (14)$$

Multiplying equation (14) by $\frac{d}{D}$ to introduce dimensionless parameter and then solving for the surface concentration leads to

$$\frac{C_s}{C_b} = \frac{1}{1 + D_{ac} / Sh} \tag{15}$$

Where Sh is defined in equation (7) and

$$D_{ac} = \frac{P_e d}{D} \tag{16}$$

2.1.3 Reactive Wall

Figure 2 shows a schematic diagram of fluid-phase solute transport to a vessel wall. The endothelial cells are shown conceptually, aligned in the longitudinal direction of the flow field with intercellular clefts elongated in the direction of flow.

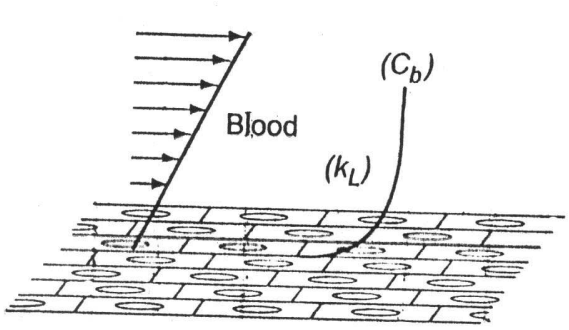

Fig.2. Schematic diagram of fluid-phase solute transport to a vessel wall.

The concentration profile of a solute being transported from the blood is shown where C_b is its bulk concentration. The fluid-phase mass transport to the cleft is characterized by the mass-transfer coefficient K_L. The intercellular clefts are assumed to be the only route for the solute uptake. Oxygen is transported readily across the endothelium, but unlike most protein, it is rapidly consumed by the underlying tissue. In this case, endothelial transport resistance is neglected (assume $C_w = C_s$), and then equating the rate of transport to the wall with the (zeroeth order) consumption rate,

$$K_l (C_b - C_s) = QT \tag{17}$$

For a specific case of O_2 transport, concentration (C) is replace with partial pressure (P) through the Henry's law relationship, C = KP, and invoking this relationship and rearranging equation (17) into a dimensionless rate

$$\frac{P_s}{P_b} = 1 - D_{aw} / sh \tag{18}$$

$$D_{aw} = \frac{QTd}{KDP_b} \tag{19}$$

Clearly, when $D_{aw} << sh,$ the process is wall limited. But, as $D_{aw} \to sh$, the process becomes limited by transport in the fluid phase ($P_s \to 0$) and fluid mechanics plays a role.

3. Results

The mathematical modeled equations describing the mass transport processes to the entire endothelial cell surface which enhances the development of atherosclerosis in arteries were developed. The Damkholer numbers for the reactive surface D_{ar}, the permeable surface $D_{ac,}$ and the reactive wall D_{aw} were solved analytically. The solved model of the transport processes verified our assumption that the reaction rate is pseudo-first order kinetics. Our aim is to show that the developed equations produce results that are similar to the measured results. All parameters used in simulation are shown in Table 1. The lengths and diameters were based on magnetic resonance measurements. At locations were measured data are not available, concentrations were estimated from combined literature data with measured and computed data [5-8].

Table 1. Parameters use for the simulation.

Parameters	**Units**
Tight junction a	10nm
Wall shear rate γ	$1000s^{-1}$
Diffusion coefficient D	2.06×10^{-7} cm^2/s
Diameter of artery d	2.5cm – large artery with sh = 1495 5μm – small artery with sh = 0.299
Volume flux or superficial Velocity J_v	$1.0\text{-}5.0 \times 10^{-6}$cm/s
Permeability coefficient P_e	0.5-2.5 mm/s
Tissue thickness T	0.5-1.1 μm for heparinase treatment plasma labeling, and hematocrit measurement
Protein concentration – Plasma phospholipids transfer protein PLTP	4.9-20.5mg/l. No sex difference observed
HDL-cholesterol	γ= 0.72; P<0.001
Apolipoprotein (apo) A-1	γ = 0.62; P<0.001
HDL_2-cholesterol	γ = 0.72; P<=0.001
Triacylycerol	γ = -0.45; P<0.0001 (negatively correlated)

Total plasma cholesterol concentration (LDL)	< 200mg/100ml considered desirable, values of 200-239mg/100ml are considered with high risk
Henry's law constant for gases dissolved in water	44,380Pa at 25^{o}C
Reynolds number R_e	250 Dimensionless
Schmidt number S_c	3000 dimensionless for both ATP or free oxygen in blood
Sherwood number sh	114 for LDL, 79.2 for albumin, 41.8 for ATP and 31.1 for oxygen
Concentration gradient at the arterial wall	0.15126d at the outlet, 0.02d in the radial direction, and 0.0056d at the circumference
Blood flow rate:	
Experimental value	$1.9278\times10^{-3}\,m^3/sm^3$ tissue
Predicted value	$1.7278\times10^{-4}-2.7897\times10^{-4}\,m^3/sm^3$ tissue
Average value	$5\times10^{-4}\,m^3/sm^3$ tissue under basal resting condition
Heat generation rate in tissue:	
Predicted value	$3.2336\times10^{2}-5.2309\times10^{2}\,w/m^3$
Average value	$4.0342\times10^{2}\,w/m^3$
Average oxygen level	$0.17m^3O_2/m^3$ blood
Oxygen of heat generation	$2.09\times10^{7}\,J/m^3$

4. Discussion of Results

The results shown in Table 2 are Damkholer numbers for the transport processes in human arteries, obtained using the model equations which are similar to those derived from estimation techniques (literature values) for low-density lipoprotein (LDL) and oxygen transport as shown in Table 3. The Damkholer numbers for albumin and LDL show that fluid-phase transport of these solutes to intercellular junctions is not a limiting factor in arteries, but may be important in capillaries.

Table 2. Damkholer number from mathematical model (simulated)

Parameter	LDL	Albumin	ATP	Oxygen
D_{ac}	1.214	-	-	-
D_{ar}	-	-	-	7.762
D_{aw}	-	-	-	14.58

Table 3. Measured Damkholer numbers for the transport processes in human arteries

Damkholer Numbers	LDL	Albumin	ATP	Oxygen
D_{ac}	0.02-1.0	0.027-0.10	-	-
D_{ar}	-	-	17.7	-
D_{aw}	-	-	-	10.8-49.0

But it is clear that since the Damkholer numbers is much greater than Sherwood number the process is termed “transport-limited” or “fluid-phase-limited”. Hence, the modeled equations are true representative of the biological system. However, a synthesis of these basic mass transport processes in relation to pattern of macromolecular uptake improve the localization of atherosclerosis and is presented in the form of several plausible mechanisms of atherogenesis in which mass transport plays a central role. High-molecular-weight species, such as LDL and albumin, are not limited by the fluid phase. Oxygen transport, however, may be fluid-phase limited in regions of low fluid-phase mass transfer rates (Sherwood number-sh), such as the outer walls of bifurcations and the inner walls of curved vessels where enhance LDL uptake and atherosclerotic lesions localize. Hypoxia in such regions has been confirmed by direct measurement in the carotid bifurcations, around vascular graft anastomoses and in other vessels. Hypoxia in the arterial wall has for many years been implicated in the development of atherosclerosis. Local hypoxia can affect the uptake of LDL and other macromolecules by the arterial wall through several mechanisms: (a) Hypoxia can break down the endothelial barrier and form interendethelial gaps leading to increased macromolecular transport. (b) Hypoxia also induces endothelial cell apoptosis, which can increase LDL transport through leaky junctions. The uptake of LDL is controlled by the endothelium, not the fluid phase, and leaky junctions, not tight junctions, would appear to constitute the principal pathway for transport of LDL across the endothelial layer. Leaky junctions are associated with cell in a state of turn over (mitosis) or death (apoptosis), and these processes are affected by local fluid mechanics. Elevated steady shear stress tends to suppress both mitosis and apoptosis, whereas low shear stress is separated or disturbed flow increase in these processes. Therefore, it is expected that leaky junctions would be more prevalent in regions of low shear stress and separated flow than in regions of higher, uni-directional shear stress. These are precisely the regions where atherosclerotic plaques tend to be localized at the carotid bifurcation, in coronary arteries, and the aortic bifurcation. For large macromolecules, such as LDL, that have a low endothelial permeability (P_e) relative to volume flux (J_v), an increase in J_v with fixed P_e will reduce the accumulation of solute beyond the endothelial layer (intima/media), by convectively clearing (flushing) out the region beyond the high resistance endothelial barrier. If we assume that a macromolecule crosses the endothelial primarily through leaky junctions, and that volume flux (primarily water flux) is controlled principally by the intercellular junctions that have a much greater total area than the leaky junctions, then factors that affects J_v but not P_e can influence the accumulation of macromolecules within the wall.

5. Conclusion

The accumulation of Lipoprotein in the arterial intima is a hallmark of atherosclerosis. Low density-lipoprotein (LDL) is the most abundant atherogentic lipoprotein in plasma and high plasma levels of LDL are casually related to the development of atherosclerosis. The results of the analysis indicated that there were no significant difference between the model derived values of the Damkholer numbers and the corresponding values simulated. Model values ($D_{ar} = 17.7$ for ATP, $D_{ac} = 0.02 - 1.0$ for LDL, $0.027 - 0.10$ for albumin, $D_{aw} = 10.8 - 49.0$ for oxygen) and simulated value ($D_{ar} = 7.762$ for oxygen, $D_{ac} = 1.214$ for LDL, $D_{aw} = 14.58$ for oxygen). The

flux of LDL into the arterial wall depends on the plasma concentration and permeability, P_e which for human aorta is between the range of $5\times10^{-4} - 2.5\times10^{-3} m/s$. Thus, a correlation between P_e and plasma concentration then enhances the localization of atherosclerotic plaques.

Research has improved our understanding of this disease, which necessitated the evaluation of the mathematical models equations for mass transport in arteries. The mathematical models in turn are used to suggest better treatments, such as administration of aspirin to reduce the risk to blood clots forming on the damaged artery lining and surgical treatment such as coronary angioplasty, which improve the quality of the patients suffering from this disease.

Nomenclature

$J_s =$ Species flux
$K_l =$ Mass transfer coefficient
$C_b =$ Bulk concentration
$C_s =$ Surface concentration
$V =$ Michaelis-Menten kinetics rate
$V_{\max} =$ Maximum rate
$K_m =$ Michaelis constant
$K_r =$ Surface reaction rate
$Sh =$ Sherwood number
$D_{ar} =$ Damkholer number
$d =$ Diameter
$D =$ Diffusion coefficient
$P_e =$ Permeability coefficient
$C_w =$ Wall concentration
$D_{ac} =$ Damkholer number based on endothelial permeability
$Q =$ Tissue consumption rate
$T =$ Tissue thickness
$K =$ Henry's law constant
$P_s =$ Surface partial pressure
$P_b =$ Bulk partial pressure
$D_{aw} =$ Damkholer number based on the wall consumption

References

[1] Kaazempur-Mofrad, M.R, Wada, S. Myers, J.G, Ethier, C.R (2005), Mass transport and fluid flow in stenotic arteries: Internal journal of heat and mass transfer 48:4510- 4517.

[2] Caro, C.G, and Nerem, R.M (1973), Transport of $^{14}C-4-cholesterol$ between serum and wall in common Carotid artery, circ. Res. 32: 187 – 205.

[3] Nerem, R. (1995), Atherosclerosis and the role of wall shear stress, Oxford University Press, New York.
[4] John, M. Tarbell (2003), Mass transport in arteries and the localization of atherosclerosis; city college, New York. Pp. 80-110
[5] Diller K.R. and Hayes L.J. (1991), Analysis of tissue injury by burning: comparison of in situ and skin flap models. IJHMT 34, 1393-1406.
[6] Krauchi K. and Wirz-Justice A. (1994), Circadian Rhythm of heat production, heart rate, and skin and core temperature under unmasking conditions in men. American Journal of Physiology 36, R819-R829.
[7] Simanti, R. U. & Ayodeji, A. J. (2003), A Noninvasive Technique to Determine Peripheral Blood Flow and Heat Generation in a Human Limb, Chem. Eng. Sci. 59 (2004) 4415 – 4423. pp. 4416 – 4417, 4419 – 4421.
[8] Smith, J.M. (2001), Chemical Engineering Thermodynamics, 6th Edition, McGraw-Hill, Singapore Pp. 348.