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EFFECT OF CLOPIDOGREL ON BLOOD FLOW THROUGH STENOSED ARTERY UNDER DISEASED CONDITION

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ABSTRACT

Clopidogrel is a cholesterol-lowering drug it can help to prevent more plaque from forming. In this present model the effects of Clopidogrel on viscosity of blood has been obtained. This problem of non-Newtonian and non-linear blood flow through a stenosed artery is solved numerically where the non-Newtonian rheology of the flowing blood is characterized by the generalized Power-law and Bingham plastic fluid models. The proposed model are solved and closed form expressions for the blood flow characteristics namely, velocity profile, volumetric flow rate, pressure gradient, resistance to flow, wall shear stress and apparent viscosity are derived. The effects of various parameters entering into problem are discussed with the help of graphs. It has been found that the wall shear stress and resistance to flow and viscosity increases with the non-Newtonian behavior index of the blood as well as tube radius for constant value of the stenosis height for both fluid models but these increases are comparatively small in Power-law fluid model. It has been concluded that the patients entangled to cardiovascular diseases due to blood clots can prevent by giving the regular doses of Clopidogrel in order to dilute the blood. This lowers the blood viscosity. Clopidogrel would be more helpful in the functioning of diseased arterial circulation. This work may be help in diagnosis and treatment of cardiovascular disorders as well as people working in biomedical field.

Keywords: Clopidogrel, Blood flow, Bingham Plastic Fluid, Power-law Fluid Model, Resistance to Flow, Wall Shear Stress, Stenosis Shape Parameter.

INTRODUCTION

The study of blood flow through mammalian circulatory system has been the subject of scientific research for about a couple of centuries. Like most of the problems of nature and life sciences, it is complex one due to the complicated structure of blood, the circulatory system and their constituent materials. The experimental studies and the theoretical treatments of blood flow phenomena are very useful for the diagnosis of a number of cardiovascular diseases and development of pathological patterns in human or animal physiology and for other clinical purposes and practical applications. Stenosis "*Atherosclerosis*" [Fig.1(a)] is the abnormal and unnatural growth on the arterial wall thickness that develops at various arterial locations of the cardiovascular system under diseased condition. Stenosis developed in the arteries pertaining to brain can cause cerebral strokes and the one developed in the coronary arteries can cause myocardial infarction which leads to heart failure. Everyone starts to develop some amount of stenosis as they grow older. In some people, the condition can cause complications such as a heart attack or stroke. It has been reported that the fluid dynamical properties of blood flow through non-uniform cross section of the arteries play a major role in the fundamental understanding and treatment of many cardiovascular diseases. Several researchers have studied the blood flow characteristics due to the presence of a stenosis in the tapered arteries. Blood behaves like a Newtonian fluid when it flows through larger arteries at high shear rates, whereas it behaves like a non-Newtonian fluid when it flows through narrow arteries at low shear rates. In the region of narrowing arterial constriction, the flow accelerates and consequently the velocity gradient

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near the wall region is steeper due to the increased core velocity resulting in relatively large shear stress on the wall even for a mild stenosis. The possibility that the haemodynamic factors play an important role in the genesis and proliferation of stenosis has attracted the interest of researchers to study blood flow through local constrictions during the past few decades [1-6]. An account of the most of the theoretical and experimental studies, reported so far [7-14], The analysis of blood flow through a symmetrically stenosed artery has been studied by Singh [15].

Sanyal and Maji [16] investigated the unsteady blood flow through an indented tube in presence of stenosis. Chakravarty and Datta [17] have performed rheological study on the effect of mild stenoses on the flow behavior of blood in a stenosed arterial segment. The various geometries of stenosis have been suggested by the researchers. The cosine-shaped geometry was considered and analysed with different parameters by many researchers like Young [7], Kapur [18], Chakravarty [19]. The power-law and casson fluid models with cosine-shaped geometry were discussed by Shukla [20]. A composite shaped geometry of arterial stenosis was also suggested and investigated. The bell-shaped geometry with different fluids was discussed by Misra and Shit. In all of the above studies the shape of stenosis was considered to be symmetrical about the axis as well as radius of the flow cylinder. The radially nonsymmetric stenosis has been analysed by Sanyal and Maji [16], Srivastava and Saxena [21], Srivastava [9]. The effects of shape of stenosis on the resistance to blood flow through an artery has been investigated by Haldar [22]. Due to the presence of a new parameter the formulation of our model is mathematically more general and includes the model as a special case. In the present mathematical model, a problem in which blood flow has been considered symmetrical about the axis but non- symmetrical with respect to radial co-ordinates with mild stenosed artery by introducing blood as Power-law fluid model and Bingham plastic fluid model. The effects of stenosis size, stenosis length, stenosis shape parameter on resistance to flow, wall shear stress and apparent viscosity have investigated.

Formulation of the Mathematical Model

We have considered an artery having mild stenosis. The flow of blood is assumed to be steady, laminar and fully-developed. Blood is taken as a Bingham plastic fluid. It is assumed that stenosis is symmetrical about the axis but non- symmetrical with respect to radial co-ordinates. The mathematical expression for geometry can be written as,

$$\left.\begin{aligned} \frac{R(z)}{R_0} &= 1 - A[L_0^{(m-1)}(z-d) - (z-d)^m], && d \le z \le d + L_0 \\ &= 1, && \text{otherwise,} \end{aligned}\right\} \quad (1)$$

$$A = \frac{\delta}{R_0 L_0^m} \frac{m^{m/(m-1)}}{(m-1)},$$

where

R_0 : Radius of normal tube

$R(z)$: Radius of stenotic region

L : The length of the artery

L_0 : The length of the stenosis

d : Distance between equispaced points

δ : Maximum height of stenosis ($\delta << R_0$)

m : Parameter determining the shape of stenosis ($m \ge 2$)

Conservation equation and boundary conditions

The equation of motion for laminar and incompressible, steady, fully-developed, one-dimensional flow of blood whose viscosity varies along radial direction in an artery reduces to:

$$\left.\begin{aligned} 0 &= -\frac{\partial P}{\partial r} + \frac{1}{r}\frac{\partial (r\tau)}{\partial z}, \\ 0 &= -\frac{\partial P}{\partial r}, \end{aligned}\right\} \quad (2)$$

where (z, r) are co-ordinates with z measured along the axis and r measured normal to the axis of the artery.The boundary conditions are introduced to solve the above equations,

$$\left.\begin{aligned} &\partial u/\partial r = 0 \quad \text{at } r = 0, \quad u = 0 \quad \text{at } r = R(z) \\ &\tau \ \text{ is finite} \quad \text{at } r = 0 \\ &P = P_0 \quad \text{at } z = 0, \quad P = P_L \quad \text{at } z = L \end{aligned}\right\} \quad (3)$$

Bingham plastic fluid model

For Bingham plastic fluid, the stress-strain relation is given by

$$\tau = \tau_0 + \mu\left(-\frac{du}{dr}\right) \quad (4)$$

$$\text{where} \quad \tau = \left(-\frac{dp}{dz}\frac{r}{2}\right), \ \tau_0 = \left(-\frac{dp}{dz}\frac{R_P}{2}\right),$$

u : axial velocity

□ : viscosity of fluid

$(-dp/dz)$: pressure gradient

Solution of the problem

The expression for the velocity, u obtained as the solution of equation (2) subject to the boundary conditions (3) and equation (4), is obtained as (for $R_P \le r \le R(z)$)

$$u = -\frac{R_0^2}{4\mu}\frac{dp}{dz}\left[\left(\frac{R}{R_0}\right)^2 - \left(\frac{r}{R_0}\right)^2\right] + \frac{\tau_0 R_0}{\mu}\left[\left(\frac{R}{R_0}\right) - \left(\frac{r}{R_0}\right)\right] - \frac{4R_0^{3/2}\tau_0}{3\mu}\left(-\frac{1}{2\mu}\frac{dp}{dz}\right)^{1/2}\left[\left(\frac{R}{R_0}\right)^{3/2} - \left(\frac{r}{R_0}\right)^{3/2}\right] \quad (5)$$

The constant plug flow velocity, u_P may be obtained from equation (5) evaluated at $r = R_P$.
The volumetric flow rate Q can be defined as,

$$Q = \int_0^R 2\pi u r\, dr = \pi \int_0^R r\left(-\frac{du}{dr}\right) dr,$$

(6)
The flow flux, Q when Rp<< R (i.e., the radius of the plug flow region is very small as compared to the non-plug flow region), is calculated as

$$Q = -\frac{R_0^4 \pi}{8\mu}\frac{dp}{dz}\left(\frac{R}{R_0}\right)^4 +- \frac{\tau_0 \pi}{3\mu}\left(\frac{R}{R_0}\right)^3 +- \frac{4R_0^{7/2}\pi}{7}\left\{\frac{\tau_0}{\mu}\left(-\frac{1}{2\mu}\frac{dp}{dz}\right)\left(\frac{R}{R_0}\right)^7\right\}^{1/2} \quad (7)$$

$$Q = \frac{\pi R^4}{8\mu}\left(-\frac{dp}{dz}\right) f(\bar{y}),$$

(8)
From above equation pressure gradient is written as follows,

$$\left(-\frac{dp}{dz}\right) = \frac{8\mu Q}{\pi R_0^4} f(\bar{y}) \quad (9)$$

$$f(\bar{y}) = \left(\bar{y}\right)^4 +- \frac{\tau_0 \pi}{3\mu}\left(\bar{y}\right)^3 +- \frac{4R_0^{7/2}\pi}{7}\left\{\frac{\tau_0}{\mu}\left(-\frac{1}{2\mu}\frac{dp}{dz}\right)\left(\bar{y}\right)^7\right\}$$

Integrating equation (9) using the condition (3) $P = P_0$ at z = 0 and $P = P_L$ at z = L. We have

$$\Delta P = P_L - P_0 = \frac{8\mu Q}{\pi R_0^4}\int_0^L \frac{dz}{\left(R(z)/R_0\right)^4 f(\bar{y}(z))} \quad 10)$$

The resistance to flow is denoted by λ and defined as follows,

$$\lambda = \frac{P_L - P_0}{Q} \quad (11)$$

The resistance to flow from equation (11) using equations (10) is written as,

$$\lambda = 1 - \left(L_0/L\right) + \left(f_0/L\right)\int_d^{d+L_0} \frac{dz}{(R(z)/R_0)^4 f(\bar{y}(z))} \quad (12)$$

where f_0 is given by

$$f_0 = \left(R/R_0\right)^4 +- \frac{\tau_0 \pi}{3\mu}\left(R/R_0\right)^3 +- \frac{4R_0^{7/2}\pi}{7}\left\{\frac{\tau_0}{\mu}\left(-\frac{1}{2\mu}\frac{dp}{dz}\right)\left(R/R_0\right)^7\right\}$$

Following the apparent viscosity (μ_{app}) is defined as follows;

$$\mu_{app} = \frac{1}{\left(R(z)/R_0\right)^4 f(\bar{y})}$$

(13)
The shearing stress at the wall can be defined as;

$$\tau_R = \tau_0 + \mu\left(-\frac{du}{dr}\right)_{r=R(z)}$$

(14)

RESULTS AND DISCUSSION

In order to have estimate of the quantitative effects of various parameters involved in the analysis computer codes were developed and to evaluate the analytical results obtained for resistance to blood flow, apparent viscosity and wall shear stress for normal and diseased system associated with stenosis due to the local deposition of lipids have been determine. Fig.2 reveals the variation of resistance to flow (λ) with stenosis size (δ/R_0) for different values of flow behavior index (n). It is observed that the resistance to flow (λ) increases as stenosis size (δ/R_0) increases. It is also noticed here that resistance to flow (λ) increases as flow behavior index (n) increases. It is seen from the Fig.2, Fig.3 that the ratio is always greater than 1 and decreases as n decreases from unity. This result is similar with the result of Shukla, et al.

In Fig.3, resistance to flow (λ) decreases as stenosis shape parameter (m) increases and maximum resistance to flow (λ) occurs at (m = 2), i. e. in case of symmetric stenosis. This result is therefore consisting to the result of [Haldar, (20)]. It is also seen that, for $\delta/R_0 = 0.1$ and $L_0/L = 1.0$ In Fig.4 the variation of wall shear stress (τ) with stenosis length (L_0/L) for different values of flow behavior index (n) has been shown. This figure depicts that wall shear stress (τ) increases as stenosis length (L_0/L) increases. Also it has been seen from this graph that the wall shear stress (τ) increases as value of flow behavior index (n) increases. As the stenosis grows, the wall shearing stress (τ) increases in the stenotic region. It is also noted that the shear ratio given is greater than one and decreases as n decreases (n < 1). These results are similar with the results of Shukla, et al.. It is also seen that the shear ratio is always greater than one and decreases as n decreases. For $\delta/R_0 = 0.1$ the increases in wall shear due to stenosis is about 37% when compared to the wall shear corresponding to the normal artery in the Newtonian case (n = 1), but for n = 2/3 this increase is only 23% approximately. However, for $\delta/R_0 = 0.2$, the corresponding increase in Newtonian (n = 1) and non-Newtonian (n = 2/3) cases are 95% and 56% respectively. Fig.5 reveals the variation of apparent viscosity with stenosis shape parameter for different values of stenosis size. It may be observed here that the apparent viscosity decreases as stenosis shape parameter increases. This figure is also depicted that apparent viscosity decreases as stenosis size increases.

Power-law fluid: Non-Newtonian fluid is that of power-law fluid which have constitutive equation,

$$\left.\begin{aligned}\left(-\frac{du}{dr}\right)=\left(\frac{\tau}{\mu}\right)^{1/n} &= f(\tau),\\ \text{where } \tau=\left(-\frac{dp}{dz}\right)\frac{R_c}{2}&\end{aligned}\right\} \quad (15)$$

Where u is the axial velocity, μ is the viscosity of fluid, (-dp/dz) is the pressure gradient and n is the flow behaviour index of the fluid. Solving for u from equation (15), (4) and using the boundary conditions (3), we have,

$$\frac{du}{dr}=\left(\frac{P}{2\mu}\right)^{1/n}[(r-R_C)^{1/n}], \quad (16)$$

The volumetric flow rate Q can be defined as,

$$Q=\int_0^R 2\pi u r\,dr=\pi\int_0^R r\left(-\frac{du}{dr}\right)dr, \quad (17)$$

By the help of equations (15) and 1(6) we have,

$$Q=\left(\frac{P}{2\mu}\right)^{1/n}\left(\frac{n\pi}{(3n+1)}\right)(R)^{[(1/n)+1]} \quad (18)$$

From equation (18) pressure gradient is written as follows,

$$\frac{dp}{dz}=-2\mu\left(\frac{(3n+1)}{n\pi}Q\right)^n\frac{1}{(R)^{3n+1}} \quad (19)$$

Integrating equation (19) using the condition $P = P_0$ at $z = 0$ and $P = P_L$ at $z = L$. We have,

$$P_L-P_0=\left(\frac{(3n+1)}{n\pi}Q\right)^n\frac{2\mu}{(R_0)^{3n+1}}\int_0^L\frac{dz}{\left(R/R_0\right)^{1+3n}} \quad (20)$$

The resistance to flow (resistive impedance) is denoted by λ and defined as follows:

$$\lambda=\frac{P_L-P_o}{Q} \quad (21)$$

The resistance to flow from equation (21) using equations (20) can write as:

$$\lambda_0=\left(\frac{(3n+1)Q}{n\pi}\right)^n\frac{2\mu}{QR_0^{3n+1}}\left(\int_0^d dz+\int_0^{d+L_0}\frac{dz}{\left(R/R_0\right)^{3n+1}}+\int_{d+L_0}^{L}dz\right) \quad (22)$$

When there is no stenosis in artery then $R = R_0$, the resistance to flow,

$$\lambda_N=\left(\frac{(3n+1)}{n\pi}Q\right)^n\frac{2\mu}{QR_0^{3n+1}}L \quad (23)$$

From equation (22) and (23) the ratio of (λ_0 / λ_N) is given as;

$$\lambda=\frac{\lambda_0}{\lambda_N}=1-\frac{L_0}{L}+\frac{1}{L}\int_d^{d+L_0}\frac{dz}{\left(R/R_0\right)^{3n+1}} \quad (24)$$

Now the ratio of shearing stress at the wall can be written as;

$$\frac{\tau_R}{\tau_N}=\left(\frac{R_0}{R}\right)^{-3n} \quad (25)$$

$$\tau=\frac{\tau_R}{\tau_N}=\frac{1}{\left(1-\frac{\delta}{R_0}\right)^{3n}} \quad (26)$$

Fig.6 reveals the variation of resistance to flow (λ) with stenosis shape parameter (m) for different values of stenosis size (δ/R_0). It is observed that the resistance to flow (λ) decreases as stenosis shape parameter (m) increases and maximum resistance to flow (λ) occurs at (m = 2), i. e. in case of symmetric stenosis. It has also been seen from this graph that resistance to flow (λ) increases as stenosis size (δ/R_0) increases. These results are therefore consisting to the result of Mishra and Verma. Fig.7 shows the variation of wall shear stress (τ) with stenosis size for different values of stenosis length (L_0/L). It is clear from the figure that the wall shear stress (τ) increases as stenosis size and stenosis length increases. These results are consistent to the observation of Haldar. The variation of apparent viscosity with stenosis length (L_0/L) for different values of stenosis size (δ/R_0) has been depicted in Fig.8. This figure shows that the of apparent viscosity increases as stenosis size (δ/R_0) increases. This result is similar to the results of Sanyal and Maji.

Fig. 1(a). Atherosclerosis

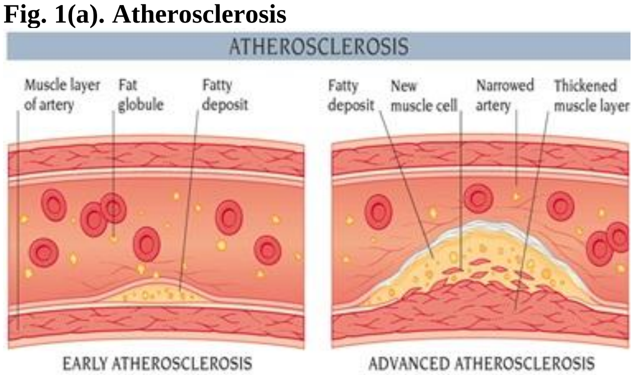
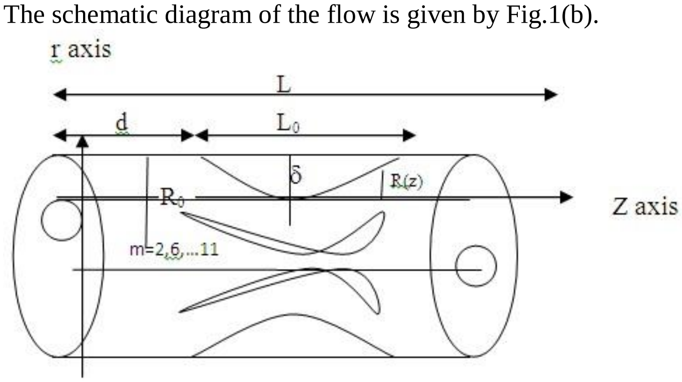


Fig.1(b). Stenotic Artery

The schematic diagram of the flow is given by Fig.1(b).



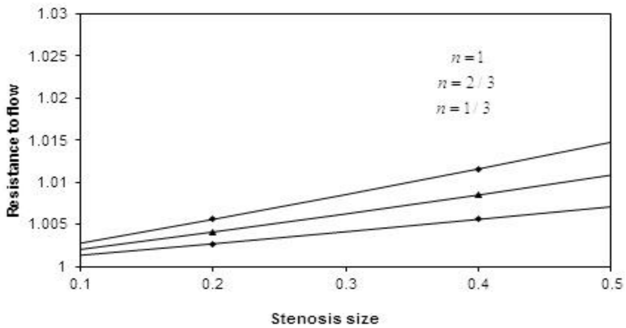


Fig 2. Variation of resistance to flow with stenosis size for different values of n

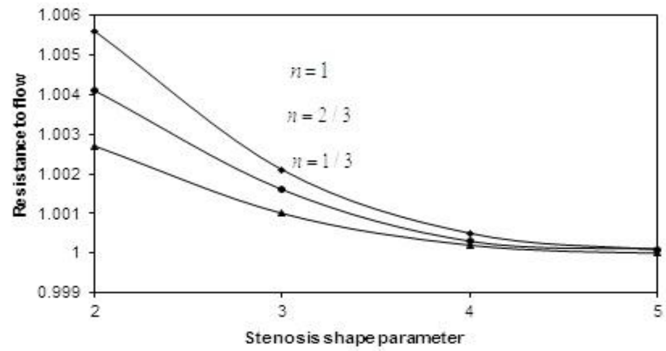


Fig 3. Variation of resistance to flow with stenosis shape parameter for n

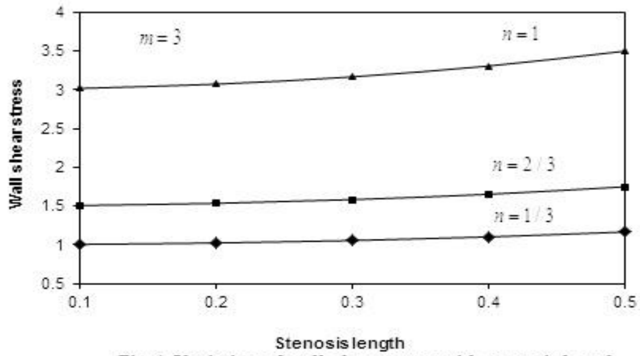


Fig 4. Variation of wall shear stress with stenosis length for different values of n

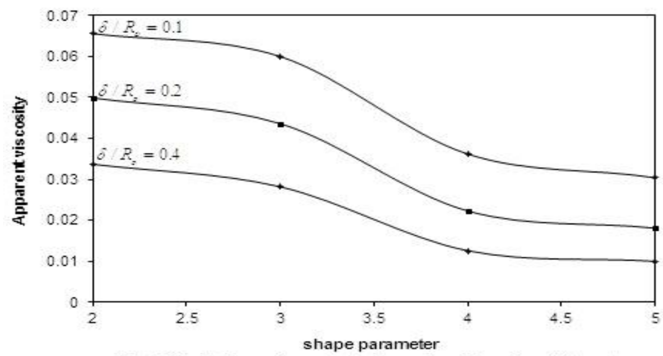


Fig 5. Variation of apparent viscosity withm for different values of stenosis size

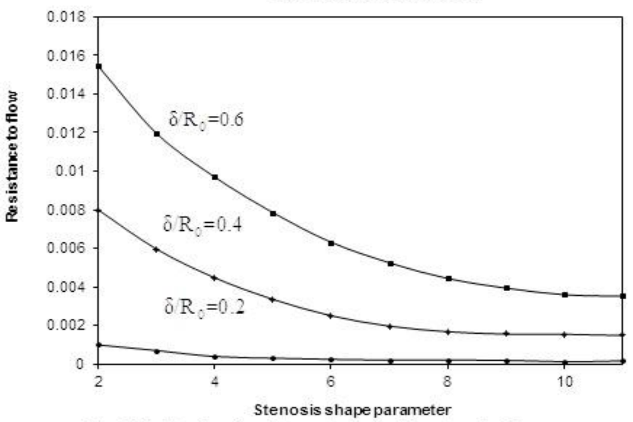


Fig 6.Variatuin of resistance to flow with stenosis shape parameter

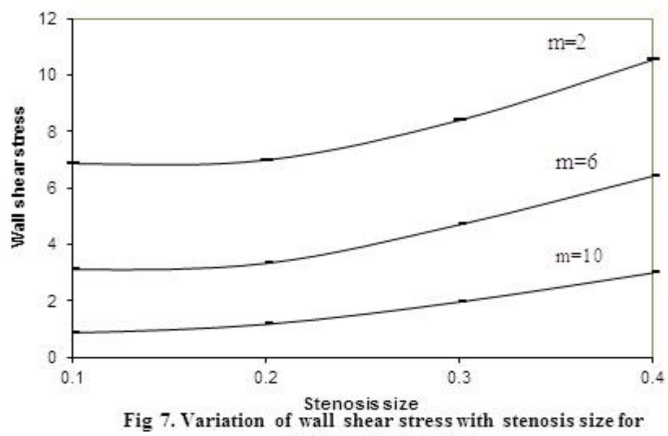


Fig 7. Variation of wall shear stress with stenosis size for different values of m

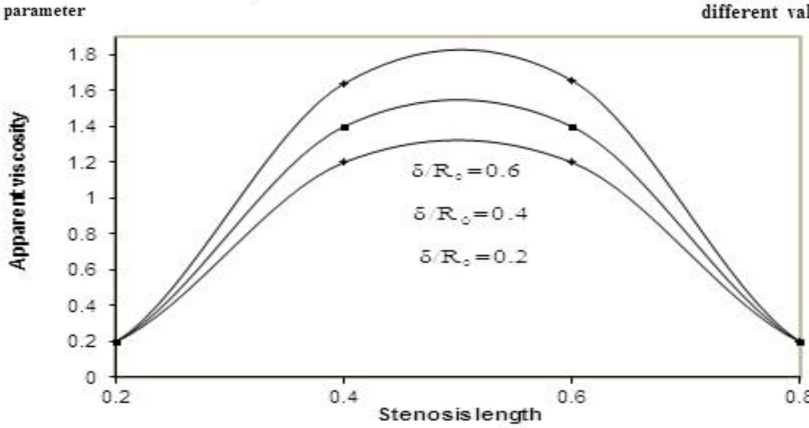


Fig 8. Variation of apparent viscosity with stenosis length

CONCLUDING REMARKS

In this paper, we have studied the effects of the stenosis in an artery by considering the blood as Power-law and Bingham plastic fluid models. It has been concluded that the resistance to flow and wall shear stress increases as the size of stenosis increases for a given non-Newtonian model of the blood. The flow resistance decreases with increasing values of shape parameter 'm' and attains its maximal in the symmetric stenosis case (m=2) for any given stenosis size. Thus the increasing value of the shape parameter would cause a considerable increase in the flow of blood. These increases are however, small due to non-Newtonian behaviour of the blood. The apparent viscosity increase as stenosis size and stenosis length increases, but it is decreases as stenosis shape parameter increases. The changes are different in both the cases of fluid models. By considering blood as power-law fluid model the flow characteristics are more favourable in comparison to Bingham plastic fluid model. Thus it appears that the non-Newtonian behaviour of blood by considering blood as power-law fluid model is more helpful in the functioning of stenosed blood vessels circulation. It has been concluded that the patients entangled to cardiovascular diseases due to the formation of blood clots can prevent by giving the regular doses of Clopidogrel in order to dilute the blood. This drug can help to prevent more plaque from forming and lowers the blood viscosity. Clopidogrel would be more helpful in the functioning of diseased arterial circulation. This work may help in early identification, diagnosis and treatment of cardiovascular disorders and also for the people working in the field of medical science.

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