Research Article

Effects of Mucus Visco-elasticity, Cilia Beating and Porosity Parameter on Mucus Transport in Human Lung Airways

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Abstract
In this paper, a two-layer circular steady state mathematical model is presented to study the mucus transport in the human lung airways by taking into account the effects of cilia beating as well as porosity parameter incorporated due to certain immotile cilia forming porous matrix bed in the serous sub-layer in contact with the epithelium. The effect of shear stress due to air motion at the mucus-air interface is also taken in the model. The serous layer fluid is considered as incompressible Newtonian fluid while mucus layer is considered as a visco-elastic fluid. The serous layer fluid is divided into twosub-layers, one in contact with the epithelium and the other in contact with themucus

Keywords: Mucus transport, Cilia Beating, Porosity, Mucus visco-elasticity.
2010 Mathematics Subject Classification:76A05,76A10,76D05,76D10,92B05

1.Introduction

The human body is supposed to be complex system which consists of many sub-systems(organs).All these systems play significant role in maintaining homeostasis and sustaining our life. The muco-ciliary system is one of the most important primary defense mechanisms of the human lung airways for cleaning the inspired air of contaminants and for the removing entrapped particles such as bacteria, viruses, cellular debris, carcinogens in tobacco smoke, etc. from the lungs through mucus transport. It consists of three layers namely: a mucus layer, a serous layer and the cilia which are small hair- like projection lining with the epithelium of the human respiratory tracts. The serous layer fluid is considered as a Newtonian fluid while mucus as visco-elastic fluid. It has been pointed out that, in general, mucus transport depend upon the structure of cilia, the function imparted by cilia tips in the serous sub-layer fluid, the thicknesses and the viscosities of the serous fluid and mucus and the interaction of mucus with the serous layer fluid.

In recent decades, the mucus transport in the human lungs has been studied by several researchers. Barton and Raynor (1967) present an analytical model for mucus transport by considering cilium as an oscillating cylinder with a greater height during the effective stroke and smaller height during the recovery stroke. Black(1975) has considered the two layer Newtonian fluid model, one serous layer fluid and other mucus and pointed out the importance of gravity and effect of air flow on mucus transport. Another mathematical analysis of two layer fluid model is given by Black and Winet(1980).They suggested that if cilia just penetrate the upper, much more viscous layer, then the mucus transport rate would be substantially enhanced.

King et al.(1993) have presented a planar two layer fluid model for muco-ciliary transport in the respiratory tract due to cilia beating and air motion by considering mucus as a viscoelastic fluid and shown that the mucus transport increases as the shear stress due to air motion, pressure drop and mean velocity of cilia tip increase. They have shown that mucus transport rate will be maximum at some value of serous fluid thickness for fixed total path of serous layer fluid and mucus.

Besides above, several investigators have studied and analysed mucus transport in human lung airways under different conditions[Verma(2010), Verma and Tripathi(2011), Verma and Rana (2015), Saxena and Tyagi(2015), Saxena et al.(2020) and many others].In view of above, in this paper, we have taken a two layer, (serous and mucus layer) circular steady state mathematical model. Here, serous fluid is taken as Newtonian fluid while mucus as visco-elastic fluid.

2.Mathematical Formulation

In real situation, the airways in the human lung are cylindrical in nature. Therefore, the physical situation of movement in the lung is idealized by circular tube geometry, the inner surface wall being ciliated [Fig.1] and it is assumed that the central lumen is filled with air surrounded by mucus (a highly viscous fluid), which is covered by a watery serous layer fluid with much lower viscosity than
that of the mucus.

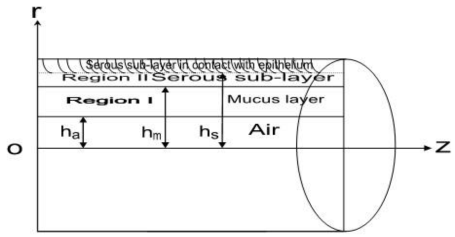

Figure 1: A circular model for mucus transport

The serous layer fluid is assumed to be divided in two sub-layers; one in contact with the epithelium and other in contact with the mucus. It is assumed that cilia during beating impart a velocity at the mean level of their tips, causing the serous sub - layer in contact with mucus to undergo motion and certain cilia are immotile and form a porous matrix bed in serous sublayer in contact with the epithelium, where flow may occur due to pressure gradient as considered by Beavers and Joseph (1967).
No net flow is assumed in the serous sub layer in contact with epithelium. The effect of air- motion is incorporated by prescribing the shear stress at the mucus air interface as a boundary condition [Blake (1975)]. The effects of pressure gradient and gravitational force are also taken into consideration in the model. The equations governing the transport of mucus and serous layer fluid under the steady state and low Reynolds number flow approximations by taking the effect of gravitational force into account in the direction of flow, are written as follows [Blake (1975), King et al. (1993)]:

Region-I: Mucus layer ($h_a \le r \le h_m$):

$$\frac{\partial \tau_m}{\partial r} = \frac{\partial p}{\partial x} - \rho_m g \cos\alpha \qquad (1)$$

$$\mu_m \frac{\partial u_m}{\partial r} = \tau_m \left[1 + \lambda^2 \left(\frac{\partial u_m}{\partial r}\right)^2\right] \qquad (2)$$

Region-II: Serous layer ($h_m \le r \le h_s$):

$$\frac{\mu_s}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u_s}{\partial r}\right) = \frac{\partial p}{\partial z} - \rho_s g \cos\alpha \qquad (3)$$

where p is the pressure that is constant across the fluid layers,u_m and u_s are the velocity component of the mucus and serous layer fluid respectively in z-direction; ρ_m,μ_m and ρ_s,μ_s are their respective densities and viscosities; g is the acceleration due to gravity, α is the angle by which the airway under consideration is inclined with the vertical;h_a, h_m and h_s are the thickness measured from the central axis OZ to the mucus-air interface, serous-mucus interface and interface between the two serous sub layers respectively as shown in the Fig.1. λ (=$\frac{\mu_m}{G}$) the relaxation time, G is the shear modulus of elasticity and τ_m is the shear stress in the mucus layer.

The boundary and matching conditions for the governing equations are taken as fallows:

Boundary conditions

$$\tau_m = \tau_a, \qquad r = h_a \qquad (4)$$

$$u_s = U_0 + \beta\frac{\partial u_s}{\partial r}, \qquad r = h_s \qquad (5)$$

where τ_a is the prescribed shear stress at the mucus-air interface which incorporates the effect of air-motion,U_0 is the mean velocity of cilia tips and β is the porosity parameter whose dimension is same as that of fluid layer thickness. The condition (4) implies that the shear stress is continuous at the mucus-air interface and incorporates the effect of air motion similar to the analysis of Blake (1975). Condition (5) implies that certain cilia beat and some cilia are immotile which form a porous matrix bed.

Matching conditions

$$u_m = u_s = U_1, \qquad r = h_m \qquad (6)$$

$$\tau_m = \mu_s\frac{\partial u_s}{\partial r}, \qquad r = h_m \qquad (7)$$

where U_1 is the mucus-serous layer interface velocity to be determined by using condition(7).The conditions (6) and (7) imply that the velocities and shear stresses are continuous at the mucus-serous layer interface.

3. Analytical Solution

Solving (1)-(3) and using boundary and matching conditions (4)-(7), we get

$$u_s=\frac{\phi_s}{4\mu_s}\left[(r^2-h_m^2)+\frac{(h_s^2-h_m^2-2\beta h_s)}{\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}}\ln\left(\frac{r}{h_m}\right)\right]+\frac{U_1\frac{\beta}{h_s}+\ln(\frac{r}{h_s})-U_0\ln\left(\frac{r}{h_m}\right)}{\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}} \quad (8)$$

and

$$u_m=\frac{\phi_m}{2\mu_m}(r^2-h_m^2)+\frac{1}{\mu_m}(\tau_a-\phi_m h_a)(r-h_m)$$
$$+\frac{\lambda^2}{4{\mu_m}^3\phi_m}[\{\tau_a-\phi_m(r-h_a)\}^4-\{\tau_a-\phi_m(h_m-h_a)\}^4]+U_1 \quad (9)$$

where

$$U_1=\frac{1}{\mu_s}\{\tau_a+\phi_m(h_m-h_a)\}\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}h_m$$
$$-\frac{\phi_s}{4\mu_s}\left\{2h_m^2+\frac{(h_s^2-h_m^2-2\beta h_s)}{\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}}\right\}\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}+U_0 \quad (10)$$

and $\phi_s=\frac{\partial p}{\partial x}-\rho_s g\cos\alpha,\quad \phi_m=\frac{\partial p}{\partial x}-\rho_m g\cos\alpha$ (11)

The volumetric flow rate i.e. flux in the two layers are respectively defined as follows:

$Q_s=\int_{h_m}^{h_s}2\pi r u_s dr$ and $Q_m=\int_{h_a}^{h_m}2\pi r u_m dr$

which after using (8) and (9) are found as:

$$Q_s=\frac{\pi\phi_s}{8\mu_s}(h_s^2-h_m^2)^2-\frac{\pi\phi_s(h_s^2-h_m^2-2\beta h_s)}{8\mu_s\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\},}\{(h_s^2-h_m^2)+2h_s^2\ln(\frac{h_m}{h_s})\}$$
$$+\frac{\pi U_1}{2\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}}\left[-(h_s^2-h_m^2-2\beta h_s)-2h_m^2\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}\right]$$
$$-\frac{\pi U_0}{2\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}}\{(h_s^2-h_m^2)+2h_s^2\ln(\frac{h_m}{h_s})\} \quad (12)$$

and

$$Q_m=\frac{\pi\phi_s}{8\mu_s}\left[2\beta h_s-h_s^2+h_m^2\left\{1-2\left(\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right)\right\}\right](h_m^2-h_a^2)$$
$$-\frac{\pi\phi_m}{4\mu_m}(h_m^2-h_a^2)^2+\frac{\pi h_m}{\mu_s}\{\tau_a+\phi_m(h_m-h_a)\}\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}(h_m^2-h_a^2)$$
$$+\frac{\pi}{3\mu_m}(\tau_a-\phi_m h_a)\{2(h_m^3-h_a^3)-3h_m(h_m^2-h_a^2)\}$$
$$+\frac{\pi(h_m^2-h_a^2)^2}{60\mu_m G^2}\left[\begin{array}{c}-2\phi_m^3(h_m^2-h_a^2)^3\{5(h_m-h_a)+12h_a\}+18\phi_m^2\tau_a\\(h_m-h_a)^2\{2(h_m-h_a)+5h_a\}-15\phi_m{\tau_a}^2(h_m-h_a)\\\{3(h_m-h_a)+8h_a\}-20{\tau_a}^3\{(h_m-h_a)-3h_a\}\end{array}\right] \quad (13)$$

It can be seen by using equation of fluid continuity that Q_s and Q_m are constants, therefore, from equation (12) and (13), we note that $-\frac{\partial p}{\partial x}$ is also constant. Hence, replacing it by the pressure drop over the length L of the cilia beating zone including the cilia forming porous matrix bed zone, the expressions for the fluxes may be written as

$$Q_s=-\frac{\pi\phi_{s0}}{8\mu_s}(h_s^2-h_m^2)^2+\frac{\pi\phi_{s0}(h_s^2-h_m^2-2\beta h_s)}{8\mu_s\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}}\left[(h_s^2-h_m^2)+2h_s^2\ln(\frac{h_m}{h_s})\right]$$
$$+\frac{\pi U_1}{2\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}}\left[-(h_s^2-h_m^2-2\beta h_s)-2h_m^2\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}\right]$$
$$-\frac{\pi U_0}{2\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}}[(h_s^2-h_m^2)+2h_s^2\ln(\frac{h_m}{h_s}) \quad (14)$$

and

$$Q_m=\frac{\pi\phi_{s0}}{8\mu_s}\left[h_s^2-2\beta h_s-h_m^2\left\{1-2\left(\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right)\right\}\right](h_m^2-h_a^2)$$
$$+\frac{\pi\phi_{m0}}{4\mu_m}(h_m^2-h_a^2)^2+\frac{\pi h_m}{\mu_s}\{\tau_a-\phi_{m0}(h_m-h_a)\}\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}(h_m^2-h_a^2)$$
$$+\frac{\pi}{3\mu_m}(\tau_a+\phi_{m0}h_a)\{2(h_m^3-h_a^3)-3h_m(h_m^2-h_a^2)\}$$
$$+\frac{\pi(h_m^2-h_a^2)^2}{60\mu_m G^2}\left[\begin{array}{c}2\phi_{m0}^3(h_m^2-h_a^2)^3\{5(h_m-h_a)+12h_a\}+18\phi_{m0}^2\tau_a\\(h_m-h_a)^2\{2(h_m-h_a)+5h_a\}+15\phi_{m0}{\tau_a}^2(h_m-h_a)\\\{3(h_m-h_a)+8h_a\}-20{\tau_a}^3\{(h_m-h_a)-3h_a\}\end{array}\right] \quad (15)$$

where

$$U_1 = \frac{1}{\mu_s}\{\tau_a - \phi_{m0}(h_m - h_a)\}\left\{\frac{\beta}{h_s} + \ln(\frac{h_m}{h_s})\right\}h_m$$

$$+\frac{\phi_{s0}}{4\mu_s}\left\{2h_m^2 + \frac{(h_s^2 - h_m^2 - 2\beta h_s)}{\left\{\frac{\beta}{h_s}+\ln(\frac{h_m}{h_s})\right\}}\right\}\left\{\frac{\beta}{h_s} + \ln(\frac{h_m}{h_s})\right\} + U_0 \qquad (16) \text{ and}$$

$$\phi_{s0} = \left(\frac{\Delta p}{L} + \rho_s g\cos\alpha\right) \ , \ \phi_{m0} = \left(\frac{\Delta p}{L} + \rho_m g\cos\alpha\right) \qquad (17)$$

where $\Delta p = p_0 - p_{L,}$ $p = p_0$at x = 0, $\Delta p = p_L$at x = L . It is noted that the effect of gravitational force due to gravity is similar to that of the pressure drop.

4.Result and Discussion

To study the effect of various parameters on mucus transport rate quantitatively, the expression for Q_m given by (15) using the value of U_1 from (16), can be written in non-dimensional form as:

$$\bar{Q}_m = \frac{\pi\bar{\phi}_{s0}}{4\bar{\mu}_s}\left[1 - 2\bar{\beta} - \bar{h}_m^2\left(\bar{\beta} + \ln\bar{h}_m\right)\right]\left(\bar{h}_m^2 - \bar{h}_a^2\right) + \frac{\pi\bar{\phi}_{m0}}{4\bar{\mu}_m}\left(\bar{h}_m^2 - \bar{h}_a^2\right)^2$$

$$+\frac{\pi\bar{h}_m}{\bar{\mu}_s}\{\bar{\tau}_a - \bar{\phi}_{m0}\left(\bar{h}_m - \bar{h}_a\right)\}\left(\bar{\beta} + \ln\bar{h}_m\right)\left(\bar{h}_m^2 - \bar{h}_a^2\right)$$

$$+\frac{\pi}{3\bar{\mu}_m}\left(\bar{\tau}_a + \bar{\phi}_{m0}\bar{h}_m\right)\{2\left(\bar{h}_m^3 - \bar{h}_a^3\right) - 3\left(\bar{h}_m^2 - \bar{h}_a^2\right)\}$$

$$+\frac{\pi}{60\bar{\mu}_m\bar{G}^2}[2\bar{\phi}_{m0}^3\left(\bar{h}_m^2 - \bar{h}_a^2\right)^3\{5\left(\bar{h}_m - \bar{h}_a\right) + 12\bar{h}_a\}$$

$$+18\bar{\phi}_{m0}^2\bar{\tau}_a\left(\bar{h}_m^2 - \bar{h}_a^2\right)^2\{3\left(\bar{h}_m - \bar{h}_a\right) - 5\bar{h}_m\}$$

$$+15\bar{\phi}_{m0}\bar{\tau}_a{}^2\left(\bar{h}_m - \bar{h}_a\right)\{3\left(\bar{h}_m - \bar{h}_a\right) + 8\bar{h}_a\}$$

$$-20\bar{\tau}_a{}^3\{\left(\bar{h}_m - \bar{h}_a\right) + 3\bar{h}_a\}]\left(\bar{h}_m^2 - \bar{h}_a^2\right)^2 \qquad (18)$$

by using the following non-dimensional parameters:

$$\bar{\beta} = \frac{\beta}{h_s}, \bar{h}_e = \frac{h_e}{h_s}, \bar{h}_s = \frac{h_s}{h_s}, \bar{\mu_s} = \frac{\mu_s}{\mu_0}, \bar{\mu}_m = \frac{\mu_m}{\mu_0}, \bar{\phi}_{s0} = \frac{\phi_{s0}h_s^2}{\mu_0 U_0},$$

$$\bar{\phi}_{m0} = \frac{\phi_{m0}h_s^2}{\mu_0 U_0}, \bar{\tau}_a = \frac{\tau_a h_s}{\mu_0 U_0}, \bar{G} = \frac{Gh_s}{\mu_0 U_0}, \overline{\lambda_0} = \frac{1}{\bar{G}}, \bar{Q}_m = \frac{Q_m}{h_s U_0}. \qquad (19)$$

where μ_0 is the viscosity of the serous sub layer fluid in contact withepithelium.

Expression for $\bar{Q}_m$ given by (18) is plotted in Fig. (2) to(6)using the following set of parameters which have been calculated by using typical values of various characteristics related to airways [King etal.(1993), Agarwal and Verma (1997)]:

$$\bar{\beta} = 0.01 - 0.05, \bar{h}_m = 0.996 - 0.998, \bar{h}_a = 0.952, \bar{\phi}_{s0} = 5, \bar{\phi}_{m0} = 5 - 20,$$

$$\bar{\mu_s} = 1 - 4, \bar{\mu}_m = 10 - 100, \bar{\tau}_a = 0.1 - 0.5, \overline{\lambda_0} = 0 - 0.05 \qquad (20)$$

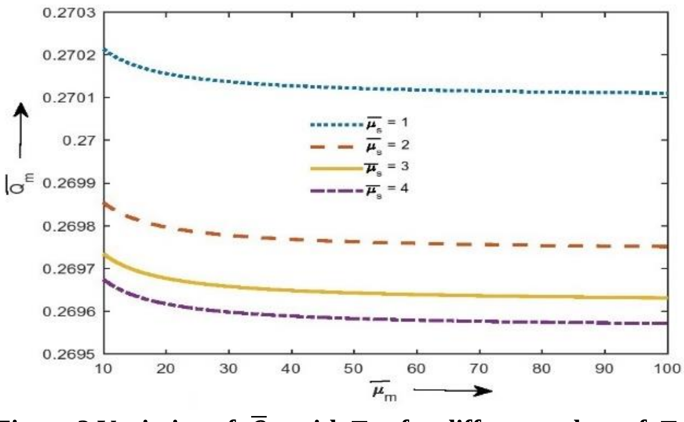

Figure.2 Variation of $\bar{Q}_m$ with $\bar{\mu}_m$ for different values of $\bar{\mu}_s$

Fig.2 shows the variation of $\bar{Q}_m$with $\bar{\mu}_m$for different values of $\bar{\mu_s}$ and for fixed values of $\bar{\beta} = 0.01$, $\bar{h}_m = 0.996$, $\bar{h}_a = 0.952$, $\bar{\tau}_a = 0.1$, $\bar{\phi}_{s0} = 5$, $\bar{\phi}_{m0} = 10$, $\overline{\lambda_0} = 0.005$.This figure illustrates that mucus transport rate decreases as the viscosity of the serous layer fluid or that of mucus increases which can be seen in the patients of cystic fibrosis which is characterised by airway mucus plugging and reduced mucus clearance [David et al. (2018)]. From figure2, it is also seen that increase in mucus viscosity at higher value do not have any significant effect on its transport rate.It has been also reported[Samet and Cheng(1994)] that mucus from bronchitis patients is more viscous during flares-up of the disease, thus the result shown in figure 2 are in line with the above findings.Thus for higher values of mucus viscosity, it behaves like an elastic slab. [Ross and corrsin(1974)].All these observations are in line with the experimental observations of King et al.(1985,1989) and analytical results of King et al.(1993), Agarwal and Verma (1997) , Verma (2010), Saxena and Tyagi(2015), Verma and Rana(2015), Saxena et al.(2020).

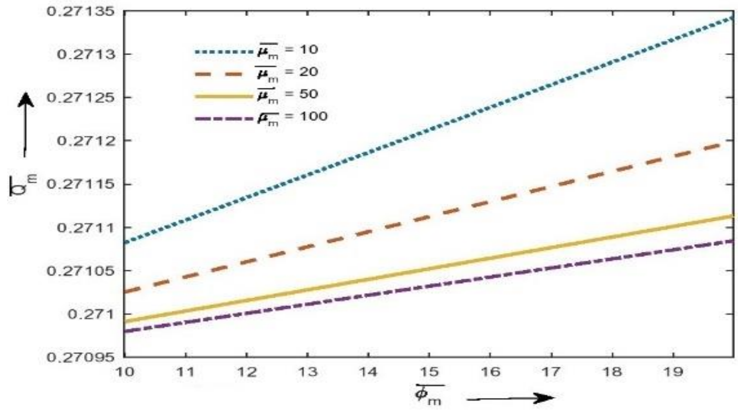

Figure.3 Variation of $\bar{Q}_m$ with $\bar{\phi}_{m0}$ for different values of $\bar{\mu}_m$

Fig.3 shows the variation of $\bar{Q}_m$ with $\bar{\phi}_{m0}$ for different value of $\bar{\mu}_m$and for fixed values of $\bar{\beta} = 0.01$, $\bar{h}_m = 0.996$, $\bar{h}_a = 0.952$, $\bar{\mu_s} = 1$, $\bar{\tau}_a = 0.1$, $\bar{\phi}_{s0} = 5$, $\overline{\lambda_0} = 0.05$. Here, it is seen that the mucus transport rate increases as the pressure drop or force due to gravity increases but it decreases with increase in mucus viscosity, the relative decrease being larger at higher values of pressure drop. This result is in line with the conclusion drawn by King et al.(1993) and Agarwal and Verma (1997) in their mathematical models.

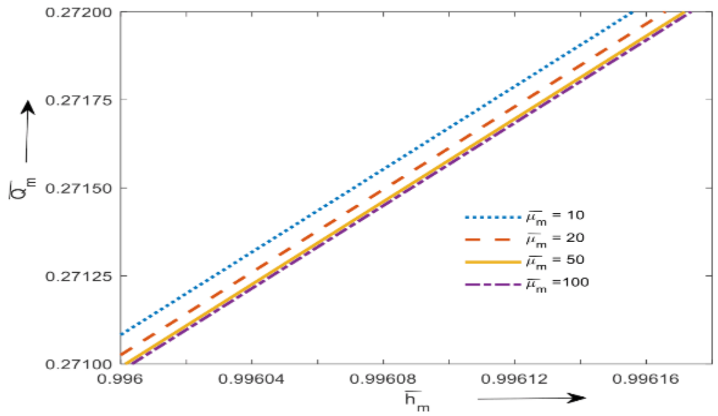

Figure.4Variation of $\bar{Q}_m$with$\bar{h}_m$ for different values of $\bar{\mu}_m$

Fig.4 shows the variation of $\bar{Q}_m$ with $\bar{h}_m$ for different values of $\bar{\mu}_m$ and fixed values of $\bar{\beta} = 0.01$, $\bar{h}_m = 0.996$, $\bar{\mu_s} = 1$, $\bar{\tau}_a = 0.1$, $\bar{\phi}_{s0} = 5$, $\bar{\phi}_{m0} = 10$, $\overline{\lambda_0} = 0.05$. This figure illustrates that mucus transport rate increases as the mucus transport rate increases as the mucus layer thickness increases. It is also seen that mucus transport rate decreases as its viscosity increases.

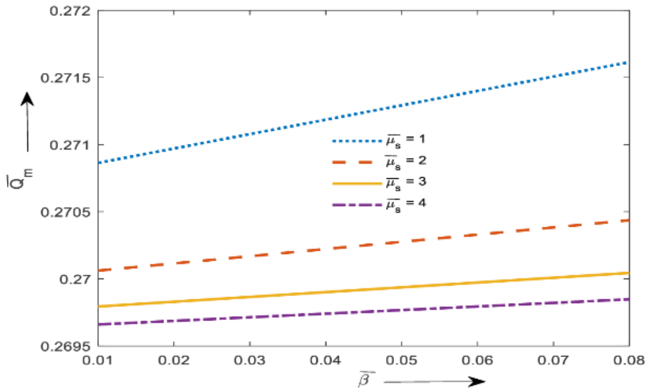

Figure.5 Variation of $\bar{Q}_m$ with $\bar{\beta}$ for different values of $\bar{\mu}_m$

Fig.5 shows the variation of $\bar{Q}_m$with $\bar{\beta}$for different values of $\bar{\mu}_s$ and for fixed values of $\bar{h}_m = 0.996, \bar{h}_a = 0.952$,$\overline{\mu_m} = 1, \bar{\tau}_a = 0.1, \bar{\phi}_{s0} = 5, \bar{\phi}_{m0} = 10, \overline{\lambda_0} = 0.05$. This figure illustrates that the mucus transport rate increases as the porosity parameter increases, but it decreases with increase in serous fluid viscosity. These observations are in line with the conclusions drawn by Agarwal and Verma (1997) and Verma (2010),Saxena and Tyagi(2015), Verma and Rana(2015) in their studies.

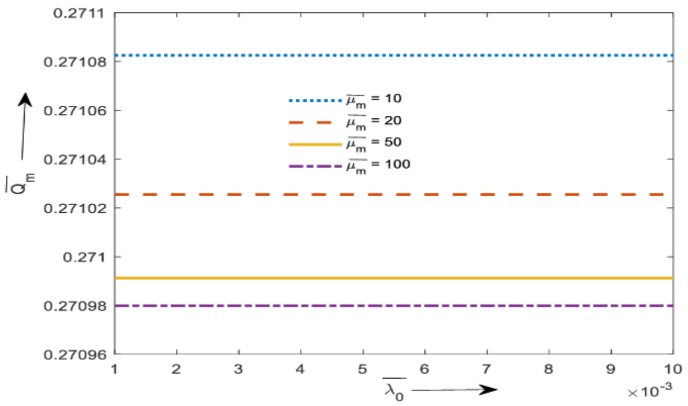

Figure.6 Variation of $\bar{Q}_m$ with $\overline{\lambda_0}$ for different values of $\bar{\mu}_m$.

Fig.6 illustrates that for the fixed values of $\bar{\beta} = 0.01$,$\bar{h}_m = 0.996, \bar{h}_a = 0.952, \overline{\mu_s} = 1, \bar{\tau}_a = 0.1, \bar{\phi}_{s0} = 5, \bar{\phi}_{m0} = 10$mucus transport rate decreases as the mucus viscosity increases. This figure also illustrates that the mucus transport rate becomes independent with$\overline{\lambda_0}$ for a fixed values of mucus viscosity, from which we conclude that the mucus transport rate decreases as its elastic modulus increases. This is in line with the analytical results of King et al.(1993), Verma and Rana(2015).

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