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Mucus and Serous Flow in Constricted Airways under the Influence of Time Varying Pressure Gradient

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Abstract

In this paper, a two-layer quasi-steady cylindrical model of mucus transport in a constricted airway under a time-varying pressure gradient due to cough is studied. Mucus is treated as an incompressible Newtonian fluid in this model. The impact of slip condition due to immotile cilia, which forms a porous matrix, is also incorporated into the model. The study notes that as the constriction thickness and serous viscosity increase, the mucus and serous flow rate decrease. Additionally, it is observed that the flow rate of mucus and serous increases as the slip parameter and pressure drop increase. It is also found that the mucus flow rate increases as the mucus thickness increase. The study also reveals that the mucus flow rates decrease as the mucus viscosity increases.

Keywords: Constricted airways, Laminar flow, Slip parameter, Time varying pressure gradient.

Mathematics Subject Classification: 74F10, 76A10, 76D10, 92B05

1. Introduction

One of the most crucial primary defence systems of the human lung airways is the muco-ciliary system, which facilitates the removal of entrapped particles from the lungs through mucus transport, including bacteria, viruses, cellular debris, and carcinogens in tobacco smoke. It is composed of three layers: the mucus layer, the serous layer, and the cilia, which are tiny projections that resemble hairs and line the bronchial respiratory tracts' epithelium. While mucus is a visco-elastic fluid, the fluid in the serous layer is thought to be Newtonian in nature. It has been noted that the structure of cilia, the roles that their tips play in the serous sub-layer fluid, and the thicknesses and viscosities of both the serous fluid and mucus are all factors that affect mucus transport in general.

Numerous researchers have examined the mucus transport in the human lungs in recent decades. Barton and Raynor [3] in particular provided an analytical model for the transfer of mucus by viewing the cilium as an oscillating cylinder that is higher during the effective stroke and lower during the recovery stroke. Blake [4] examined a two-layer Newtonian fluid model in which the fluid in the serous layer was replaced by mucus. He emphasized the impact of air flow and gravity on the movement of mucus. Blake and Winet [5] provide another mathematical study of the two-layer fluid model. They proposed that the mucus transport rate would be greatly increased if cilia could only pierce the upper, considerably more viscous layer. Even though Schroter and Sudlow [21] and Pedley et al. [13] have studied the air flow resistance in bronchial airways, many others, including Puchelle et al. [14], Zahm et al. [30], King et al. [9,10,11] in their experimental studies, have emphasized the role of mucus interaction with mucus in bronchial clearance. Experiments on coughing related to Scherer and Burtz [20] demonstrated the significance of fluid viscosity. Agarwal et al. [1] have studied the mucus transport by airflow interaction in a miniaturized simulated cough machine and found that mucus transport increases as the viscosity of the serous layer simulant decreases or as the mucus filance (spinnability) decreases. King et al. [10] also studied the interaction of airflow with the mucus gels in a simulated cough machine under steady state and oscillatory airflow conditions and emphasized the significance of mucus gel viscosity on transport. Given that mucus is a visco-elastic fluid, King et al. [11] presented a planar two-layer fluid model for muco-ciliary transport in the respiratory tract caused by cilia beating and air motion. They demonstrated that mucus transport increases with shear stress brought on by air motion, pressure drop, and mean velocity of cilia tips. It has been demonstrated that the mucus transport rate reaches its peak at a specific serous fluid thickness value, given a set total depth of both mucus and serous layer fluid.

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By taking into account the cilia bed as a porous matrix, Agarwal and Verma [2] presented a two-layer steady state mathematical model to investigate the mucus transport in the respiratory tract caused by airflow. Through the prescription of shear stress at the mucus-air interface, the effect of air motion is included in their work. Mucus transport is demonstrated to increase with pressure drop, porosity parameter increases, and shear stress brought on by air motion. Additionally, mucus transport has been shown to diminish with increasing serous layer or mucus viscosity; nevertheless, mucus transfer remains unaffected at higher mucus viscosity values. In order to study mucus transport in human lung airways, Rana et al. [16] have developed a two-layer circular steady-state mathematical model that takes into account the impacts of mucus viscoelasticity, cilia beating, and porosity parameter. Mucus transport in a diseased airway has been studied by Kumar et al. [12], who took into account the impact of constriction on the airways. It has been demonstrated that when airway diameter increases, mucus transport rate decreases. By taking into account the effect of slip parameter, Chitra and Shabana [6] have proposed a two-layer model for the air-mucus interface in the constricted human airways under a time-varying pressure gradient. They have demonstrated that when the slip parameter increases, the mucus transport rate increases as well.

In this paper, we aim to analyse a two-layer cylindrical co-axial flow model of mucus and serous in diseased airways under the influence of time varying pressure gradient. The constriction attaches to the wall penetrating into serous layer is sinusoidal. The effect of a slip parameter due to the immotile cilia bed, which forms a porous bed within which the serous fluid flows following Darcy's law is considered in the model. We use the following assumptions, as utilized in past study by other investigators:

1. The fluid flow in the cylindrical tube is symmetrical about its central axis.
2. The pressure gradient caused by coughing in the fluid layers varies over time.
3. Mucus behaves as an incompressible Newtonian fluid due to the large shear rates seen when coughing [Zahm et al. [30]].
4. During coughing, mucus and serous flow are assumed to be laminar and quasi-steady.
5. In larger airways, there may exist a slip parameter at the interface of the mucus layer and immotile cilia bed that is saturated with periciliary fluid and creates a porous matrix in accordance with Darcy's law.

2. Mathematical Model

Naturally, the airways of the human lungs appear to be cylindrical in shape. Thus, the circular tube geometry idealizes the physical conditions of movement in the lung airways. The central lumen is thought to be filled with air and encircled by a highly viscous mucus fluid, which is covered by a watery periciliary layer that has a viscosity significantly lower than that of the mucus (Fig. 1). The inner surface wall is ciliated. Presumably, some cilia are immotile and form a porous matrix bed in the periciliary layer where they come into touch with the epithelium. The impact of a slip parameter caused by immotile cilia in the periciliary layer, which create a porous matrix when in contact with the epithelium, is also taken into consideration by the model. Smooth muscles attached to the wall can cause the serous layer to contract and tighten in pathological conditions.

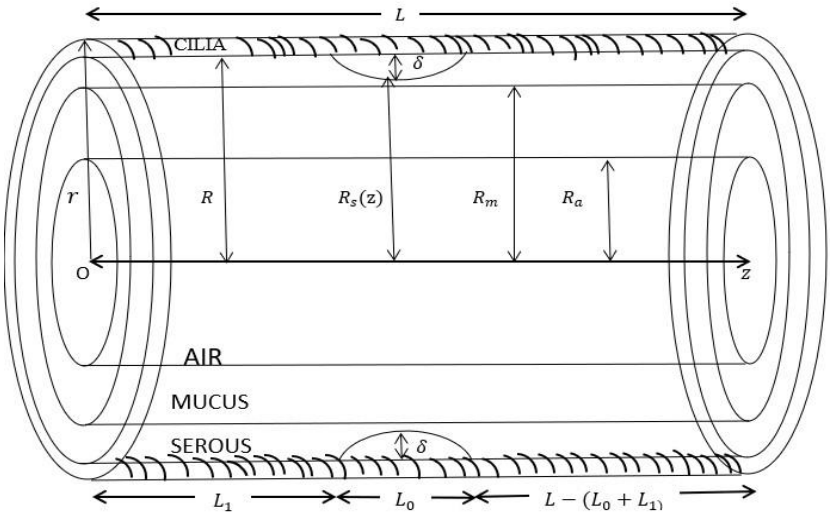

Figure 1: Circular tube geometry for mucus transport in constricted airways.

The radius of the circular tube varies based on the constriction geometry and can be described as follows [Young (1968), Shukla (1979)]:

$$\frac{R_s(z)}{R} = \begin{cases} 1 - \frac{\delta}{2R}\{1 + cos\frac{2\pi}{L_0}\left(z - L_1 - \frac{L_0}{2}\right)\}, & L_1 \le z \le L_1 + L_0 \\ 1, & 0 \le z \le L_1 \; and \; L_1 + L_0 \le z \le L \end{cases} \quad (1)$$

where R is the radius of circular tube, $R_s(z)$ is the radius of circular tube in constricted area, δ ($<< R_s(z)$) is the thickness of constriction which is sinusoidal.

Let, $a = R - \frac{\delta}{2}$ and $b = \frac{\delta}{2}$ then equation (1) becomes:

$$R_s(z) = a - bcos\frac{2\pi}{L_0}\left(z - L_1 - \frac{L_0}{2}\right)$$

The equation governing the mucus and serous flow under quasi-steady state in a circular tube can be written as follows:

Region I: Mucus Region $(\mathrm{R_a} \le \mathrm{r} \le \mathrm{R}_m)$

$$\frac{\partial p}{\partial z} = \frac{1}{r}\frac{\partial}{\partial r}(r\tau_m) \quad (2)$$

$$\tau_m = \mu_m \frac{\partial u_m}{\partial r} \quad (3)$$

Region II: Serous Region $\left(\mathrm{R}_m \le \mathrm{r} \le \mathrm{R_s(z)}\right)$

$$\frac{\partial p}{\partial z} = \frac{1}{r}\frac{\partial}{\partial r}(r\tau_s) \quad (4)$$

$$\tau_s = \mu_s \frac{\partial u_s}{\partial r} \quad (5)$$

where z is the axial coordinate along the tube axis which is in the flow direction and r is the radial coordinate in the radial direction which is perpendicular to the fluid flow, R_a is the thickness up to air-mucus interface, R_m is the thickness up to mucus-serous interface, p is the mean pressure that is constant across the two layers, τ_m and τ_s are the mean shear stress across mucus and serous region, u_m and u_s are the mean velocity components of the mucus and serous in the direction of z and μ_m, μ_s are the viscosities of mucus and serous respectively.

The formation of porous bed by immotile cilia during mild coughing or forced expiration causes slipperiness at the boundary $r = R_s(z)$. Therefore,

Boundary Conditions:

$$u_s = -\beta\tau_s, \quad r = R_s(z) \quad (6)$$

Matching Conditions:

$$u_m = u_s, \qquad r = R_m \quad (7)$$

$$\tau_m = \tau_s, \qquad r = R_m \quad (8)$$

The negative sign in equation (6) is considered due to the negative value of τ_s in the serous layer. It is important to emphasize that β is the slip parameter at the boundary between mucus and immotile cilia, which are saturated with the periciliary layer and form a porous matrix in the airways. Equations (7) and (8) ensure that velocity and stress components are continuous at the mucus-serous interface [Singh (2021)].

The pressure gradient generated during coughing in lung airways changes with time. Therefore, we may assume that

$$-\frac{\partial p}{\partial z} = P = P_0 f(t) \quad (9)$$

where t is time, P_0 is constant and influenced by intensity of cough. The higher intensity of cough leads to proportional increase in flow rates as the flow duration progresses. The function $f(t)$ in equation (9) is taken from the paper of Satpathi et al. [1973] which is defined as follows:

$$f(t) = \begin{cases} \frac{27\, t(T-t)^2}{4T^3} & ,\ 0 \le t \le T \\ 0 & ,t > T \end{cases} \tag{10}$$

For the sake of simplicity, we may also assume that the cough duration T ranges from 0.001 sec to 0.03 sec. The graphical representation of equation (10) is shown in Figure 2.

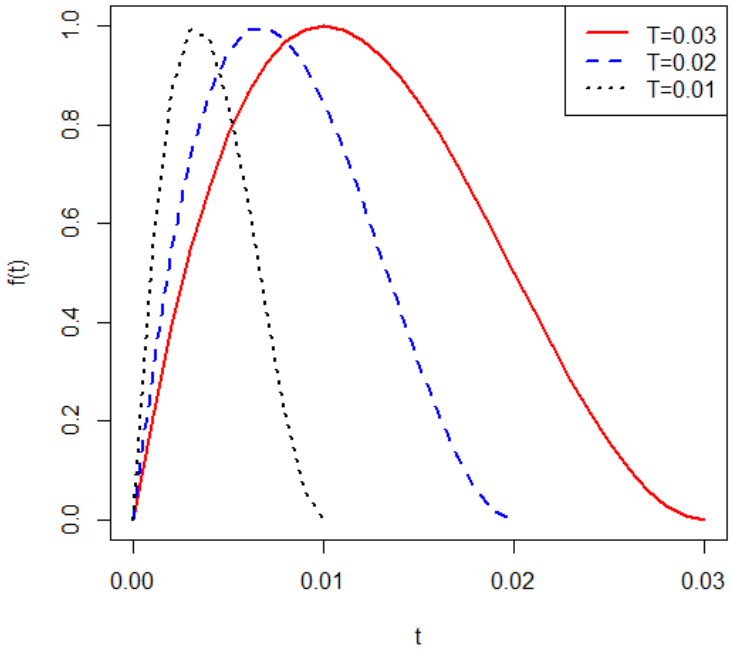

Figure 2: Graphical Representation of $f(t)$ with t for various values of T

3. Analytical Solution

Solving equations (2)-(5) by using boundary and matching conditions (6)-(8), the stress and velocity components in mucus and serous layers are computed which are given below:

$$\tau_m = \tau_s = -\frac{Pr}{2} \tag{11}$$

$$u_m = \frac{P}{4\mu_m}(R_m^2 - r^2) + \frac{P}{4\mu_s}(R_s^2(z) - R_m^2) + \frac{\beta P R_s(z)}{2} \tag{12}$$

$$u_s = \frac{P}{4\mu_s}(R_s^2(z) - r^2) + \frac{\beta P R_s(z)}{2} \tag{13}$$

The volumetric flow rates in the two layers (mucus and serous) can be defined as follows:

$$Q_m = \int_{R_a}^{R_m} 2\pi r\, u_m dr \tag{14}$$

$$Q_s = \int_{R_m}^{R_s(z)} 2\pi r\, u_s dr \tag{15}$$

Substituting the values of u_m from (12) and u_s from (13) in equation (14) and (15) respectively, we get

$$\frac{Q_m}{2\pi} = \frac{P}{16\mu_m}\left(R_m^2 - {R_a}^2\right)^2 + \frac{P}{8\mu_s}(R_s^2(z) - R_m^2)\left(R_m^2 - {R_a}^2\right) + \frac{P\beta R_s(z)}{4}\left(R_m^2 - {R_a}^2\right) \tag{16}$$

$$\frac{Q_s}{2\pi} = \frac{P}{16\mu_s}\left(R_s^2(z) - {R_m}^2\right)^2 + \frac{P\beta R_s(z)}{4}(R_s^2(z) - R_m^2) \tag{17}$$

To calculate the pressure drop in each layer, we understand from the equation of continuity that both Q_m and Q_s are constants. Therefore, from equation (16) and (17), we get

$$-\frac{\partial p}{\partial z}=\frac{Q_m}{2\pi K_2\left(R_s^2(z)+K_1R_s(z)-K_3\right)} \tag{18}$$

$$-\frac{\partial p}{\partial z}=\frac{Q_s}{2\pi K_4\left(R_s^2(z)-R_m^2\right)\left(R_s^2(z)+2K_1R_s(z)-R_m^2\right)} \tag{19}$$

where $K_1=2\beta\mu_s$, $K_2=\frac{R_m^2-R_a^2}{8\mu_s}$, $K_3=R_m^2\left(1-\frac{\mu_s}{2\mu_m}\right)+R_a^2$ and $K_4=\frac{1}{16\mu_s}$.

Replacing $R_s(z)$ by R for non-constricted regions, the pressure gradient for non-constricted regions $0\le z\le L_1$ and $L_1+L_0\le z\le L$ becomes

$$-\frac{\partial p}{\partial z}=\frac{Q_m}{2\pi K_2(R^2+K_1R-K_3)} \tag{20}$$

$$-\frac{\partial p}{\partial z}=\frac{Q_s}{2\pi K_4\left(R^2-R_m^2\right)\left(R^2+2K_1R-R_m^2\right)} \tag{21}$$

The pressure is present only at two ends of the tube i.e. $p=p_0$ at $z=0$, $p=p_L$ at $z=L$. Then, we define the pressure drop as $\Delta P=p_0-p_L$.

Now, integrating equations (18) and (20), we get

$$\Delta P=-\int_0^L dp=\int_0^{L_1}\left[\frac{Q_m}{2\pi K_2(R^2+K_1R-K_3)}\right]dz+\int_{L_1}^{L_1+L_0}\left[\frac{Q_m}{2\pi K_2\left(R_s^2(z)+K_1R_s(z)-K_3\right)}\right]dz+\int_{L_1+L_0}^{L}\left[\frac{Q_m}{2\pi K_2(R^2+K_1R-K_3)}\right]dz$$

Putting the value of $R_s(z)$ from (1) in above equation, we get

$$\Delta P=\frac{Q_m}{2\pi K_2}\left\{\frac{(L-L_0)}{(R^2+K_1R-K_3)}+\frac{L_0}{(n-m)}\left[\frac{1}{((a+m)^2-b^2)^{\left(\frac{1}{2}\right)}}-\frac{1}{((a+n)^2-b^2)^{\left(\frac{1}{2}\right)}}\right]\right\} \tag{22}$$

where, $m=\frac{K_1}{2}+\frac{\sqrt{K_1^2+4K_3}}{2}$ and $n=\frac{K_1}{2}-\frac{\sqrt{K_1^2+4K_3}}{2}$

The volumetric flow rate of mucus i.e.; Q_m can be found as follows:

$$Q_m=\frac{2\pi K_2\Delta P}{\frac{(L-L_0)}{(R^2+K_1R-K_3)}+\frac{L_0}{(n-m)}\left[\frac{1}{((a+m)^2-b^2)^{\frac{1}{2}}}-\frac{1}{((a+n)^2-b^2)^{\frac{1}{2}}}\right]} \tag{23}$$

Similarly, integrating equation (19) and (21), we get

$$\Delta P=-\int_0^L dp=\int_0^{L_1}\frac{Q_s\,dz}{2\pi K_4\left(R^2-R_m^2\right)\left(R^2+2K_1R-R_m^2\right)}+\int_{L_1}^{L_1+L_0}\frac{Q_s\,dz}{2\pi K_4\left(R_s^2(z)-R_m^2\right)\left(R_s^2(z)+2K_1R_s(z)-R_m^2\right)}+\int_{L_1+L_0}^{L}\frac{Q_s\,dz}{2\pi K_4\left(R^2-R_m^2\right)\left(R^2+2K_1R-R_m^2\right)}$$

Putting the value of $R_s(z)$ from (1) in above equation, we get

$$\Delta P=\frac{Q_s}{2\pi K_4}\left\{\frac{(L-L_0)}{\left(R^2-R_m^2\right)\left(R^2+2K_1R-R_m^2\right)}+\frac{L_0}{2R_m}\left[\frac{\left((a-R_m)^2-b^2\right)^{\left(-\frac{1}{2}\right)}}{(u+R_m)(v+R_m)}-\frac{\left((a+R_m)^2-b^2\right)^{\left(-\frac{1}{2}\right)}}{(u-R_m)(v-R_m)}\right]+\frac{L_0}{(u-v)}\left[\frac{\left((a+v)^2-b^2\right)^{\left(-\frac{1}{2}\right)}}{\left(v^2-R_m^2\right)}-\frac{\left((a+u)^2-b^2\right)^{\left(-\frac{1}{2}\right)}}{\left(u^2-R_m^2\right)}\right]\right\}$$

where, $u=K_1+\sqrt{K_1^2+R_m^2}$ and $v=K_1-\sqrt{K_1^2+R_m^2}$.

The volumetric flow rate of serous i.e.; Q_s can be found as follows:

$$Q_s = 2\pi K_4 \Delta P \left\{ \frac{(L-L_0)}{(R^2-R_m^2)(R^2+2K_1R-R_m^2)} + \frac{L_0}{2R_m}\left[\frac{((a-R_m)^2-b^2)^{\left(-\frac{1}{2}\right)}}{(u+R_m)(v+R_m)} - \frac{((a+R_m)^2-b^2)^{\left(-\frac{1}{2}\right)}}{(u-R_m)(v-R_m)}\right] + \frac{L_0}{(u-v)}\left[\frac{((a+v)^2-b^2)^{\left(-\frac{1}{2}\right)}}{(v^2-R_m^2)} - \frac{((a+u)^2-b^2)^{\left(-\frac{1}{2}\right)}}{(u^2-R_m^2)}\right]\right\}^{-1} \quad (24)$$

4. Results and Discussion

We have utilized the model analysis for the second generation of larger airways and examined the scenario when $R = 46.45 \times 10^{-2}$cm. To explore the impact of parameters on mucus and serous flow rates, the values of Q_m and Q_s in second generation of lungs airway as specified by equations (23) and (24) were determined using the following dataset [Weibal (1963), Shukla (1999)]:

$R = 46.45 \times 10^{-2}$ cm, l_0= 0.40 cm,

$R_m = 38.45 \times 10^{-2}$ cm, $P_0 = (1-10) \times 10^5$ gm cm^{-2} sec^{-2},

$R_a = 31.45 \times 10^{-2}$ cm, β= 0 − 0.10 gm cm^2 sec,

t= 0 − 0.035 sec, μ_m = 1.00 − 10.00 poise,

T = 0.035 sec, μ_a= 0.0002 poise,

L = 1.0 cm, μ_s = 0.01 – 0.10 poise,

L_0= 0.5 cm, δ = 0 − 0.1 cm.

The variations in volumetric flow rates Q_m and Q_s with respect to time t are shown in following figures:

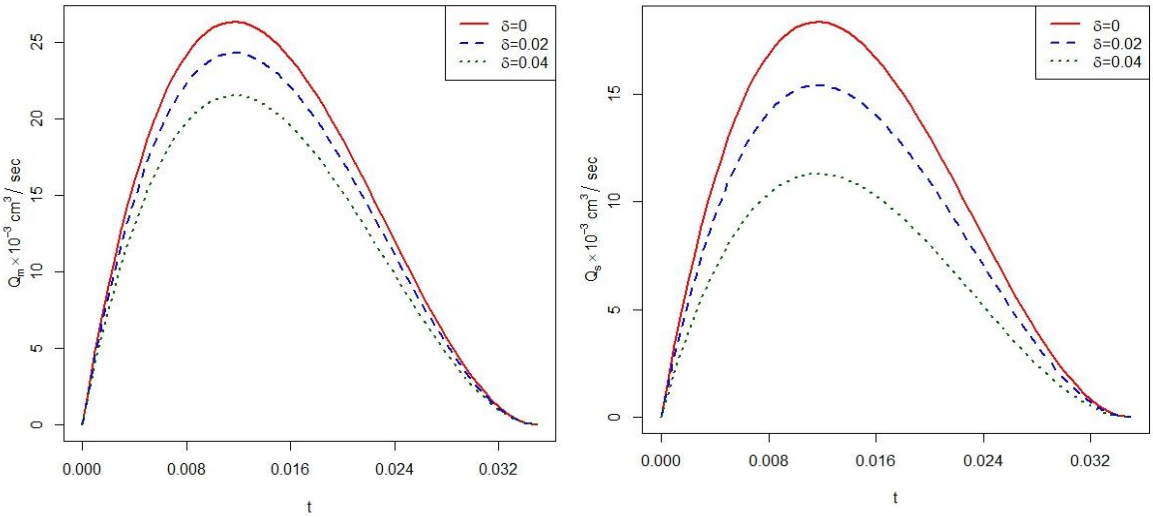

Figure 3: Variations of Q_m and Q_s with t for different values of δ

For fixed values of T = 0.035 sec, $R = 46.45 \times 10^{-2}$cm, $R_m = 38.45 \times 10^{-2}$ cm, $R_a = 31.45 \times 10^{-2}$cm, L = 1.0 cm, L_0= 0.5 cm, $P_0 = 1 \times 10^5$ gm cm^{-2} sec^{-2} , β= 0.05 gm cm^{2}sec, $\rho_a = 1.00 \times 10^{-3} gm\ cm^{-3}$, μ_m = 1 poise, μ_s = 0.01 poise and μ_a= 0.0002 poise. Figures 3 shows the effect of time on the flow rates of mucus and serous for different values of δ. It is noted that as constriction thickness increases the flow rates of mucus and serous decrease. These findings are in line with the results Chitra et al. [6], Singh et al. [24] and others.

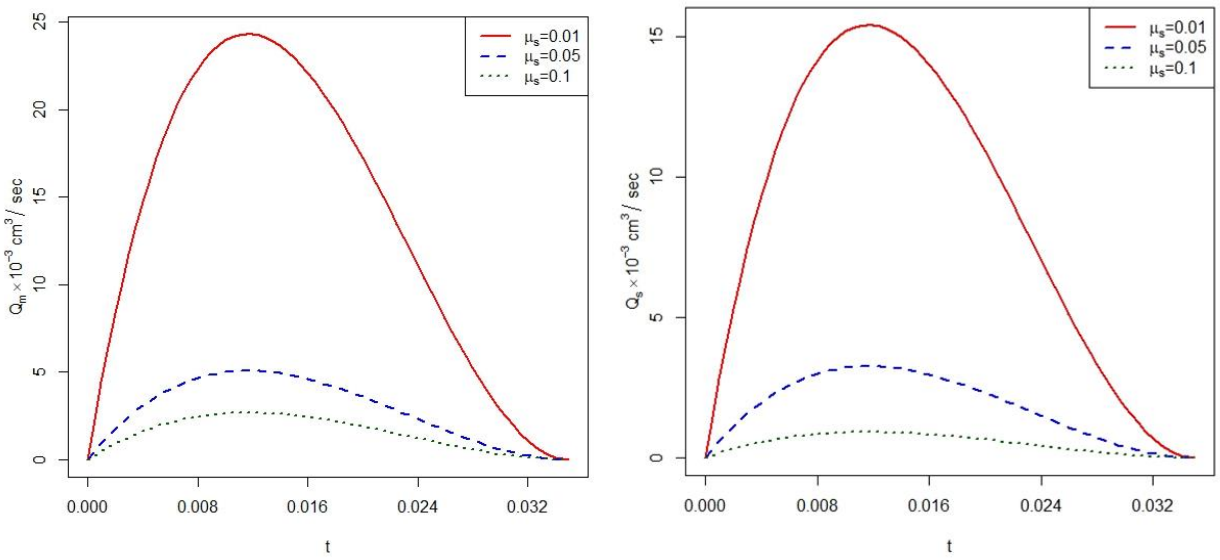

Figure 4: Variations of Q_m and Q_s with t for different values of μ_s

Figure 4 illustrate the impact of time on mucus and serous flow rates for fixed values of $R = 46.45 \times 10^{-2}$cm, $R_m = 38.45 \times 10^{-2}$ cm, $R_a = 31.45 \times 10^{-2}$cm, T = 0.035 sec, L = 1.0 cm, L_0= 0.5 cm, $P_0 = 1 \times 10^5$ gm cm^{-2} sec^{-2} , β= 0.05 gm cm^{2}sec, $\rho_a = 1.00 \times 10^{-3} gm\ cm^{-3}$, μ_a= 0.0002 poise and δ = 0.02 cm for various values of μ_s. The observation reveals that serous and mucus flow rates decrease with increase in serous viscosity. These results match with the results of Kumar et al. [12] and many others.

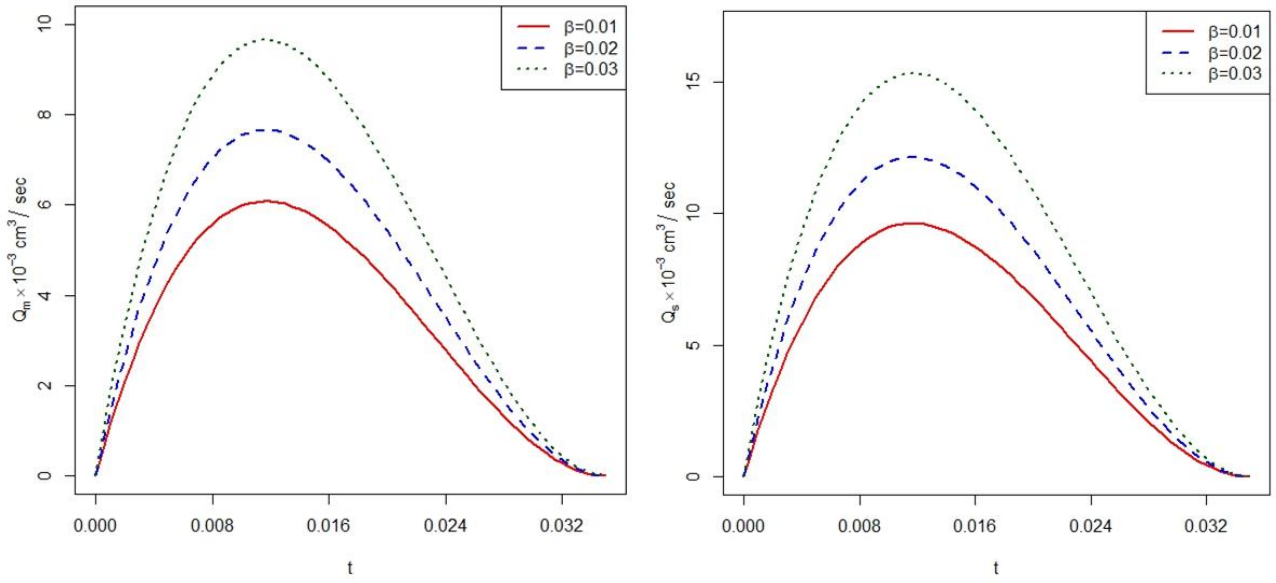

Figure 5: Variations of Q_m and Q_s with t for different values of β

Figure 5 depict the impact of time on mucus and serous flow rates for fixed values of $R = 46.45 \times 10^{-2}$cm, $R_m = 38.45 \times 10^{-2}$ cm, $R_a = 31.45 \times 10^{-2}$cm, T = 0.035 sec, L = 1.0 cm, L_0= 0.5 cm, $\rho_a = 1.00 \times 10^{-3} gm\ cm^{-3}$, $P_0 = 1 \times 10^5$ gm cm^{-2} sec^{-2} , μ_m = 1 poise, μ_a= 0.0002 poise, μ_s = 0.01 poise and δ = 0.02 cm poise for different values of β. It is observed that mucus and serous flow rates increase as the slip parameter β increases. These results match with the results of Satpathi et.al [18, 19] and others.

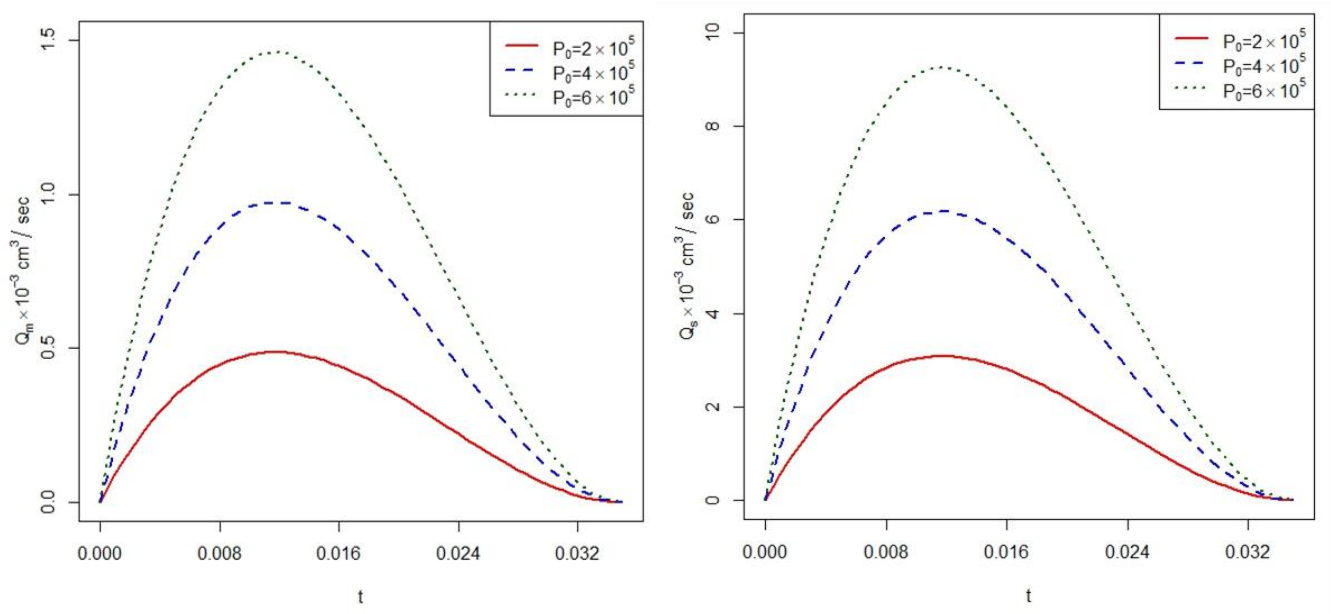

Figure 6: Variations of Q_m and Q_s with t for different values of P_0

Figure 6 depict the impact of time on mucus and serous flow rates for fixed values of $R = 46.45 \times 10^{-2}$cm, $R_m = 38.45 \times 10^{-2}$ cm, $R_a = 31.45 \times 10^{-2}$cm, T = 0.035 sec, L = 1.0 cm, L_0= 0.5 cm, β= 0.05 gm cm^{2}sec, $\rho_a = 1.00 \times 10^{-3} gm\ cm^{-3}$, μ_m = 1 poise, μ_a= 0.0002 poise, μ_s = 0.01 poise and δ = 0.02 cm for different values of P_0. It is observed that serous and mucus flow rates increase as the pressure drop in the two layers increases. These results match with the results of several investigators [1, 2, 3, 15, 20, 21].

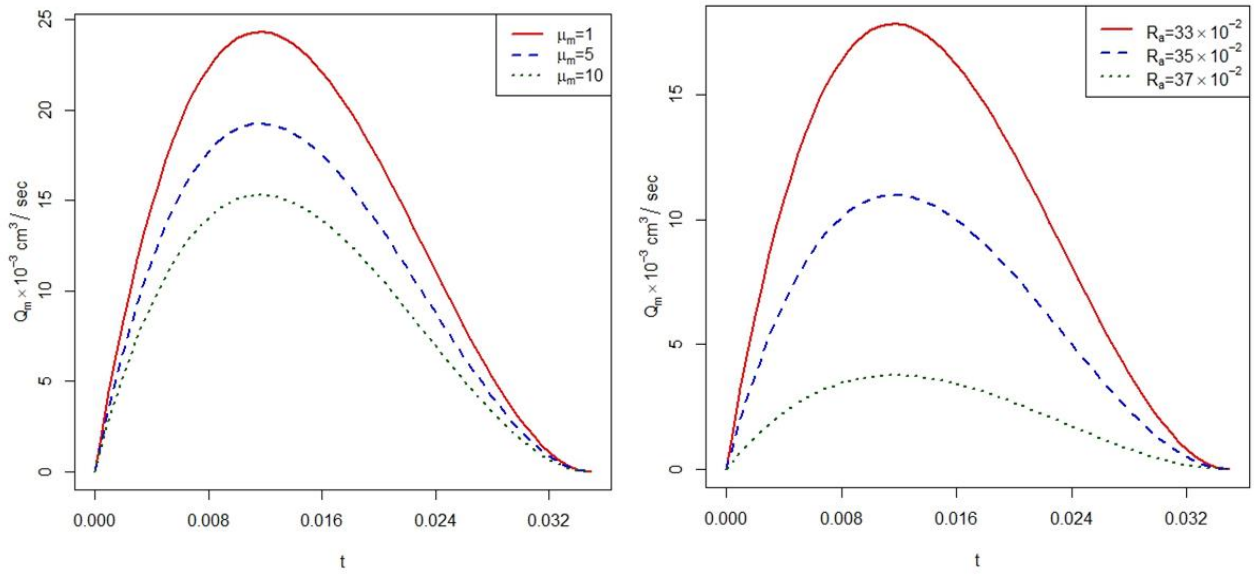

Figure 7: Variations of Q_m with t for different values of μ_m

Figure 7 illustrate the impact of time on mucus flow rate for fixed values of $R = 46.45 \times 10^{-2}$cm, $R_m = 38.45 \times 10^{-2}$ cm, T = 0.035 sec, L = 1.0 cm, L_0= 0.5 cm, $P_0 = 1 \times 10^5$ gm cm^{-2} sec^{-2} , β= 0.05 gm cm^{2}sec, $\rho_a = 1.00 \times 10^{-3} gm\ cm^{-3}$, μ_a= 0.0002 poise, μ_s= 0.01 poise and δ = 0.02 cm for various values of μ_m and R_a . The observation reveals that mucus flow rate decrease with increase in mucus viscosity. Also, noted that the mucus flow rate increases with increase in mucus thickness. These results match with the results Verma et al. [25, 26], Rana et al. [16] and many others.

5. Conclusion

The two-layer cylindrical quasi-steady co-axial flow model that is presented in this study takes into account the stresses in two layers as well as how coughing affects mucus production in constricted airways. It is assumed that the

mucus and serous flows under quasi-steady-state laminar conditions. With the boundary conditions, the model additionally incorporates the impact of the slip parameter. Graphical and analytical analysis given the following results:

a) Mucus and serous flow rates decrease with increasing constriction thickness.
b) Mucus and serous flow rates decrease as the serous viscosity increase.
c) Mucus and serous flow rates increase when the slip parameter increases.
d) Mucus and serous flow rates are increasing in coordination with an increase in pressure gradient, which is influenced by cough intensity.
e) Mucus flow rate decreases with increasing mucus viscosity and increases with greater mucus thickness.

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