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Mucus Transport in the Larger Airway Due to Prolonged Mild Cough: Effect of Serous Fluid and Cilia Beating

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Abstract
Since mucus production and transport is an important defense mechanism of the lower airways, this study focuses on this aspect. In this paper it is assumed that the co-axial flows of mucus and air is taking place in a circular tube representing a larger airway. In the central core, air is assumed to flow under quasi steady state turbulent condition and the mucus layer surrounding this central core is assumed to flow under unsteady laminar condition. The prolonged mild cough is represented by a time dependent pressure gradient function. To consider the effect of serous fluid, it has been assumed that the cilia bed is approximated by a porous matrix within which serous fluid flows following Darcy's law. Further, the effect of cilia beating has been considered by assuming that a constant mean velocity which is a resultant of effective and recovery stroke is imparted on the serous fluid and this velocity is superimposed on the Darcy flow. For constant porosity of cilia bed and mucus viscosity, it is shown that air and mucus flow rates decrease with increase in serous fluid viscosity. The effect of porosity of cilia bed and cilia beating has been found to increase the air and mucus flow rates.
Keywords Cilia Beating; Porous Matrix; Mucus Transport; Circular Model; Prolonged Mild Cough.
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1. Introduction

Nature has provided highly complex system in human body and the human lung is no exception (Grotberg 2001). The lung, the lower part of respiratory tract known as bronchial tree, a complex system of branching of tubes, starting from trachea dividing into two bronchi and continuing up to the alveoli, where the gas exchange occurs in cardiovascular system. During normal breathing, the airways transport air into the lungs and with air, also dust, toxic gases, and microorganisms are inhaled, many of which are deposited in the lower airways. Mucus production and continuous mucus transport from the lower airways to the oropharynx is an effective defense mechanisms to clear the airways of alien materials and keep the lung sterile. The airway mucus is composed of mainly long chain glycoprotein and salts in a suspension of water (Silberberg 1983, Sleigh 1981). The mucus viscosity may range from 10 Poise to 10^3 Poise at low shear rate (1 sec^{-1}) and its magnitude is about .01 Poise at high shear rate (100 sec^{-1})(King et al. 1993, Puchelle et al. 1983). Yates in 1980 considered mucus as a Newtonian fluid while some other researchers treated it as a Maxwell fluid.

The cilia are spaced uniformly along the cell surface in a relaxed hexagonal lattice and the cilia spacing is about 0.3-0.4 micrometer (Sleigh et al. 1988). The cilia perform wavy movement to remove dust and bacteria along with mucus from the airways towards the throat and thus preventing airways of the lungs from infection. Cilia beat in a coordinated wave like motion through the sol layer (Sanderson et al. 1981) thus mucus transport is governed by the mechanical forces of ciliary beating and airflow. The work done during the effective stroke is several times the amount of work done performed during the recovery stroke (Gueron 1999). The duration of effective stroke is 0.01 second. The recovery stroke lasts nearly twice as long as the effective stroke. Thus, the cilia are able to transport the mucus layer. The goblet cells produce mucus while serous cells produce serous fluid, a water like substance. The serous fluid behaves like a Newtonian fluid. Its viscosity varies from 0.01-0.1 Poise. A mixture of lipoproteins called surfactant is secreted by special surfactant cells that are part of the alveolar epithelium and bronchioles, useful in mucus transport by causing slip at the inner wall of each lung. (Sleigh et al. 1988)

In the literature, many researchers work on mucociliary transport. Recently, Smith et al. 2007 have developed a mathematical model of the transport of mucus and PCL in the airways. Some researchers studied the mucociliary transport analytically by considering a two layer fluid model, mucus being viscoelastic Maxwell fluid and serous layer as a low viscosity Newtonian liquid (e.g. Ross and Corrsin 1974, Satpathi 1998).

Once the glottis is reopened, a bi-phasic burst of air at 30-50 m/sec rapid peak, with high flow rate and a prolonged lower flow rate phase travels through the partially collapsed trachea and other airways, the flow becoming turbulent (Sleigh et al. 1988). The shearing force causes acceleration of mucus layer leading to its transport and the matter contained within it. As studied by Vander Schans et al. 1990 mucus clearance was considerably less in patients with chronic airflow obstruction and normal elastic recoil pressure than in patients with chronic airflow obstruction and decreased elastic recoil pressure. Forced expirations were less effective in treating retention of mucus in patients with low than with normal elastic recoil pressure. Smith et al. 2008 recently discussed mathematical modelling of the fluid mechanics of mucociliary clearance and introduced the morphology of the bronchial and tracheal airway surface liquid (ASL) and ciliated epithelium.

2. Governing Equations with Boundary and Matching Conditions

In view of the above considerations and using Prandtl mixing length theory, the means of quasi steady state equations in the turbulent layer and the unsteady state equations of mucus in the laminar layer can be written in cylindrical coordinates as follows (Schlichting,1960) Fig. 1 Mucus Transport in a circular tube:

Region I: Quasi steady turbulent flow of air $\left(0 \le r \le R_a\right)$:

$$-\frac{\partial p}{\partial z}+\frac{1}{r}\frac{\partial}{\partial r}\left(r\tau_a\right)=0\,; \qquad \tau_a=\rho_a l_a^2\left|\frac{\partial u_a}{\partial r}\right|\frac{\partial u_a}{\partial r}=-\rho_a l_a^2\left(-\frac{\partial u_a}{\partial r}\right)^2 \tag{1}$$

Region II: Unsteady laminar flow of mucus $\left(R_a \le r \le R_m\right)$:

$$-\frac{\partial p}{\partial z}+\frac{1}{r}\frac{\partial}{\partial r}\left(r\tau_m\right)=\rho_m\frac{\partial u_m}{\partial t}\,; \qquad \tau_m=\mu_m\frac{\partial u_m}{\partial r} \tag{2}$$

In equation (1) and (2), t is the time, z is the coordinate along the axis of the tube in the flow direction, r is the coordinate in the radial direction and perpendicular to fluid flow, R_a is the thickness up to air-mucus interface, R is the radius of the tube, p is the mean pressure which is constant across two layers, u_a , u_m are the mean velocity components of air (under turbulent flow) and mucus (under laminar flow) in the z direction respectively, τ_a is the mean shear stress in the air and τ_m is the mean shear stress in the laminar mucus layer, ρ_a and ρ_m are the densities of air and mucus respectively and μ_m is viscosity of mucus.

The mixing length $l_a = l_0$ (R-r), where l_0 is constant and determined experimentally.

Case 1.

To study the effect of serous fluid, it has been assumed that the cilia bed is approximated by a porous matrix within which serous fluid flows following Darcy's law.

Boundary conditions

$$\frac{\partial u_a}{\partial r}=0 \qquad \text{at } r=0 \tag{3}$$

$$u_m=u_s=-\frac{\phi_s}{\mu_s}\frac{\partial p}{\partial z} \qquad \text{at } r=R_m \tag{4}$$

In the region of cilia bed $(R_m \le r \le R)$ we have assumed that serous fluid is flowing following Darcy's law as cilia bed is assumed to behave like porous matrix. Here ϕ_s is the coefficient of porosity.

Case 2.

To study the effect of cilia beating it is proposed that the porous matrix formed by cilia bed is alive and active due to cilia beating and this bed moves with a mean velocity in the direction of flow. This aspect can be taken into account by changing the boundary conditions.

Boundary conditions

$$\frac{\partial u_a}{\partial r}=0 \qquad \text{at } r=0 \tag{5}$$

$$u_m=u_s=-\frac{\phi_s}{\mu_s}\frac{\partial p}{\partial z}+U_C \qquad \text{at } r=R_m \tag{6}$$

In this case, in the region of cilia bed $(R_m \le r \le R)$ to see the effect of cilia beating on mucus transport during prolonged mild cough, the cilia are assumed to be beating in a coordinated manner in such a way so that the mean velocity (resultant of effective stroke and recovery stroke) U_c is imparted on mucus in addition to the velocity in the porous bed caused by pressure gradient.

Matching conditions

$$u_a=u_m\,;\ \tau_a=\tau_m \qquad \text{at } r=R_a \tag{7}$$

Equation (7) represents the continuity of the velocity and stress components at the two interfaces.

$$-\frac{\partial p}{\partial z}=P=P_0 f(t) \tag{8}$$

Where P_0 is the strength of the prolonged mild cough, the magnitude of which depends upon the intensity of turbulence caused by prolonged mild cough and as this increases flow rates also increase. If there is no prolonged mild cough then P is zero everywhere. But still mucus transport takes place because of the mean velocity of cilia beating [Fig.2].

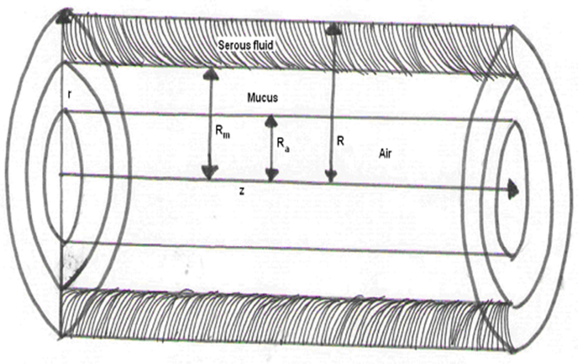

Fig. 1 Mucus Transport in a circular tube

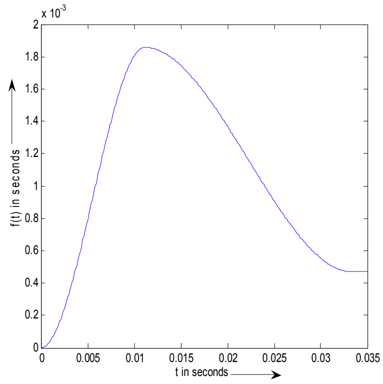

Fig. 2 Function representing Prolonged Mild Cough

The function *f(t)* in (8) is assumed to be given by,

$$f(t)=\begin{cases} \dfrac{321}{640}\dfrac{t^2}{T_m}\left(1-\dfrac{2t}{3T_m}\right) & 0\le t\le T_m \\ \dfrac{9}{32}t\left(1-\dfrac{9t}{10\,T}\right)^2+\dfrac{T}{64} & T_m\le t\le \dfrac{T}{\alpha} \\ \dfrac{T}{64} & t\ge \dfrac{T}{\alpha} \end{cases} \tag{9}$$

Where T is the duration of cough and α is the constant which is 0.9 and T_m=0.011 sec. This function represents the prolonged Mild Cough (Leith 1977)

3. Analysis of model

Case 1.

To see the effect of serous fluid viscosity we solve the model (1)-(2) using the boundary conditions (3), (4), matching conditions are given by (7). To solve the unsteady equation in laminar layer we use the method of averaging as done by Sestak and Charles in 1968.The velocity components in each layer can be found as follows:

$$u_a=\frac{\phi_s P}{\mu_s}+\left(\frac{R_m^2-R_a^2}{4\mu_m}\right)P-\frac{\rho_m\psi_m}{2\mu_m}\left(\frac{R_m^2-R_a^2}{2}+R_a^2\ln\frac{R_a}{R_m}\right) \tag{3.1}$$
$$+\frac{1}{l_0}\left(\frac{2PR}{\rho_a}\right)^{\frac12}\left[\ln\frac{R^{\frac12}+R_a^{\frac12}}{R^{\frac12}+r^{\frac12}}-\frac12\ln\frac{R-R_a}{R-r}-\frac{R_a^{\frac12}-r^{\frac12}}{R^{\frac12}}\right]$$

$$u_m=\frac{\phi_s P}{\mu_s}+\left(\frac{R_m^2-r^2}{4\mu_m}\right)P-\frac{\rho_m\psi_m}{2\mu_m}\left(\frac{R_m^2-r^2}{2}+R_a^2\ln\frac{r}{R_m}\right) \tag{3.2}$$

The volumetric flow rates in each layer can be defined as

$$Q_a=\int_0^{R_a}2\pi r u_a\,dr,\qquad Q_m=\int_{R_a}^{R_m}2\pi r u_m\,dr \tag{3.3}$$

This after using equations (3.1) and (3.2) can be written as

$$\frac{Q_a}{2\pi}=\frac{\phi_s R_a^2 P}{2\mu_s}+\left(\frac{R_m^2-R_a^2}{8\mu_m}\right)PR_a^2-\frac{\rho_m\psi_m R_a^2}{4\mu_m}\left(\frac{R_m^2-R_a^2}{2}+R_a^2\ln\frac{R_a}{R_m}\right) \tag{3.4}$$
$$+\frac{R^2}{2l_0}\left(\frac{PR}{2\rho_a}\right)^{\frac12}\left[\ln\frac{R^{\frac12}+R_a^{\frac12}}{R^{\frac12}-R_a^{\frac12}}-2\left(\frac{R_a}{R}\right)^{\frac12}\left\{1+\frac{R_a}{3R}+\frac{R_a^2}{5R^2}\right\}\right]$$

$$\frac{Q_m}{2\pi}=P\left(R_m^2-R_a^2\right)\left[\frac{\phi_s}{2\mu_s}+\frac{R_m^2-R_a^2}{16\mu_m}\right]-\frac{\rho_m\psi_m}{2\mu_m}\left(\frac{\left(R_m^2-R_a^2\right)\left(R_m^2-3R_a^2\right)}{8}-\frac{R_a^4}{2}\ln\frac{R_a}{R_m}\right) \tag{3.5}$$

Case 2.

To see the effect of cilia beating we solve the model (1)-(2) using boundary conditions (5), (6) and the matching conditions are given by (7). To solve the unsteady equation in laminar sublayer we again use the method of averaging as done by Sestak and Charles in 1968. In this case the velocity components in each layer can be found as follows:

$$u_a = \frac{\phi_s P}{\mu_s} + \left(\frac{R_m^2 - R_a^2}{4\mu_m}\right)P - \frac{\rho_m \psi_m}{2\mu_m}\left(\frac{R_m^2 - R_a^2}{2} + R_a^2 \ln\frac{R_a}{R_m}\right) + U_c + \frac{1}{l_0}\left(\frac{2PR}{\rho_a}\right)^{\frac{1}{2}}\left[\ln\frac{R^{\frac{1}{2}} + R_a^{\frac{1}{2}}}{R^{\frac{1}{2}} + r^{\frac{1}{2}}} - \frac{1}{2}\ln\frac{R - R_a}{R - r} - \frac{R_a^{\frac{1}{2}} - r^{\frac{1}{2}}}{R^{\frac{1}{2}}}\right] \tag{3.6}$$

$$u_m = \frac{\phi_s P}{\mu_s} + \left(\frac{R_m^2 - r^2}{4\mu_m}\right)P - \frac{\rho_m \psi_m}{2\mu_m}\left(\frac{R_m^2 - r^2}{2} + R_a^2 \ln\frac{r}{R_m}\right) + U_c \tag{3.7}$$

The volumetric flow rates given by (3.3) after using equations (3.6) and (3.7) can be written as

$$\frac{Q_a}{2\pi} = \frac{\phi_s R_a^2 P}{2\mu_s} + \left(\frac{R_m^2 - R_a^2}{8\mu_m}\right)PR_a^2 - \frac{\rho_m \psi_m R_a^2}{4\mu_m}\left(\frac{R_m^2 - R_a^2}{2} + R_a^2 \ln\frac{R_a}{R_m}\right) + \frac{R^2}{2l_0}\left(\frac{PR}{2\rho_a}\right)^{\frac{1}{2}}\left[\ln\frac{R^{\frac{1}{2}} + R_a^{\frac{1}{2}}}{R^{\frac{1}{2}} - R_a^{\frac{1}{2}}} - 2\left(\frac{R_a}{R}\right)^{\frac{1}{2}}\left\{1 + \frac{R_a}{3R} + \frac{R_a^2}{5R^2}\right\}\right] + \frac{U_c R_a^2}{2} \tag{3.8}$$

$$\frac{Q_m}{2\pi} = P\left(R_m^2 - R_a^2\right)\left[\frac{\phi_s}{2\mu_s} + \frac{R_m^2 - R_a^2}{16\mu_m}\right] + \frac{\left(R_m^2 - R_a^2\right)U_c}{2} - \frac{\rho_m \psi_m}{2\mu_m}\left(\frac{\left(R_m^2 - R_a^2\right)\left(R_m^2 - 3R_a^2\right)}{8} - \frac{R_a^4}{2}\ln\frac{R_a}{R_m}\right) \tag{3.9}$$

To solve the unsteady equation in laminar layer we use the method of averaging as done by Sestak and Charles in 1968.

Thus,by substituting the acceleration term on the right hand side of equation (2) by its mean value across the film thickness i.e.

$$\frac{\partial u_m}{\partial t} \approx \Psi_m = \frac{1}{R_m - R_a}\int_{R_a}^{R_m} \frac{\partial u_m}{\partial t}\, dr \tag{3.10}$$

Then equation (2) reduces to

$$\frac{\partial}{\partial r}(r\tau_m) = -(P - \rho_m \Psi_m)r \tag{3.11}$$

Where Ψ_m is a function of time only, and P as given in equation (8).

Now by differentiating Equation (3.2) or (3.7) with respect to t and using equation (3.11)

$$\psi_m' + \frac{\psi_m}{a_2} = \frac{a_1}{a_2}P' = \frac{a_1}{a_2}P_0 f'(t) \tag{3.12}$$

Where, f' denotes the derivative of function f with respect to t.

And $a_1 = \dfrac{(2R_m + R_a)(R_m - R_a)}{12\mu_m} + \dfrac{\phi_s}{\mu_s}$

$$a_2 = \frac{\rho_m}{2\mu_m}\left[\frac{(2R_m + R_a)(R_m - R_a)}{6} - R_a^2\left(1 + \frac{R_a}{R_m - R_a}\ln\frac{R_a}{R_m}\right)\right]$$

Now on solving (3.12) using (8) and (9), we get

$$
\psi_m = a_1 p_0 \exp\left(-\frac{t}{a_2}\right)
\begin{cases}
\dfrac{321}{320\,T_m^2}\left[a_2\left(2a_2+T_m\right)-\exp\left(\dfrac{t}{a_2}\right)\left(2a_2^2-2a_2t+t^2+\left(a_2-t\right)T_m\right)\right] & 0\le t\le T_m \\[2ex]
\dfrac{3}{3200\,T^2T_m^2}\left[\begin{array}{l}-2140\,a_2^2T^2\left(-1+\exp\left(\dfrac{T_m}{a_2}\right)\right)\\ -T_m\left(\begin{array}{l}-1070\,a_2\left(1+\exp\left(\dfrac{T_m}{a_2}\right)\right)T^2\\ +3T_m\left(\begin{array}{l}-\exp\left(\dfrac{t}{a_2}\right)\left(\begin{array}{l}243\left(2a_2^2-2a_2t+t^2\right)\\+360\left(a_2-t\right)T+100\,T^2\end{array}\right)\\ +\exp\left(\dfrac{T_m}{a_2}\right)\left(\begin{array}{l}486\,a_2^2+360\,a_2T\\+100\,T^2-9\left(54a_2+40T-27T_m\right)T_m\end{array}\right)\end{array}\right)\end{array}\right)\end{array}\right] & T_m\le t\le \dfrac{T}{\alpha} \\[2ex]
\dfrac{1}{3200\,T^2T_m^2}\left[\begin{array}{l}6a_2\left(\begin{array}{l}27\exp\left(\dfrac{10T}{9a_2}\right)\left(27a_2-10T\right)T_m^2\\+535\,T^2\left(T_m+2a_2\right)\end{array}\right)\\ -3\exp\left(\dfrac{T_m}{a_2}\right)\left(2140\,a_2^2T^2+T_m\left(\begin{array}{l}-1070\,a_2T^2\\+3T_m\left(\begin{array}{l}486\,a_2^2+360\,a_2T+100\,T^2\\-9T_m\left(54a_2+40T-27T_m\right)\end{array}\right)\end{array}\right)\right)\end{array}\right] & t\ge \dfrac{T}{\alpha}
\end{cases}
\tag{3.13}
$$

4. Discussion and Results

We now study the air and mucus flow rates with respect to various parameters. We apply the model analysis to the larger airways and consider the case where $R = 41.45 \times 10^{-2}$ cm. To study the effect of various parameters on air flow rate and mucus transport quantitatively the expressions for Q_a and Q_m have been calculated and plotted by using the following set of parameters (Shukla et al. 1999).

$T = .03$sec,	$t = 0\text{-}0.035$ sec,
$l_0 = l_1 = 0.40$	$R_a = 31.45\times10^{-2}$ cm,
$\mu_m = 1.00\text{-}10.00$ poise	$\rho_a = 1.00 \times 10^{-3}$ gm cm^{-3}
$\rho_m = 1.00$ gm cm^{-3}	$\phi_s = 0\text{-}0.10$ gm^{-1} cm^2 sec
$\mu_s = 0.01\text{-}0.10$ poise	$P_0 = 1 \times 10$ gm cm^{-2} sec^{-2}
$R_m = 38.45\times10^{-2}$ cm	$U_c = 0.03\text{-}0.05$ cm sec^{-1}

Figure 4.1 illustrates the effect of time on air and mucus flow rates for $\mu_m = 5$ poise, $\phi_s = 0.05$ gm^{-1} cm^2 sec and various values of μ_s and from these figures it is observed that air and mucus flow rates increases as serous fluid viscosity decreases. It is observed from Figure 4.2 that for fixed mucus and serous fluid viscosities, as the coefficient of porosity increases air and mucus flow rates increase. In figure 4.3 pressure gradient is considered to be zero to see the effect of cilia beating and hence it can be seen easily that air and mucus flow rate increases as the mean velocity of cilia beating increases.

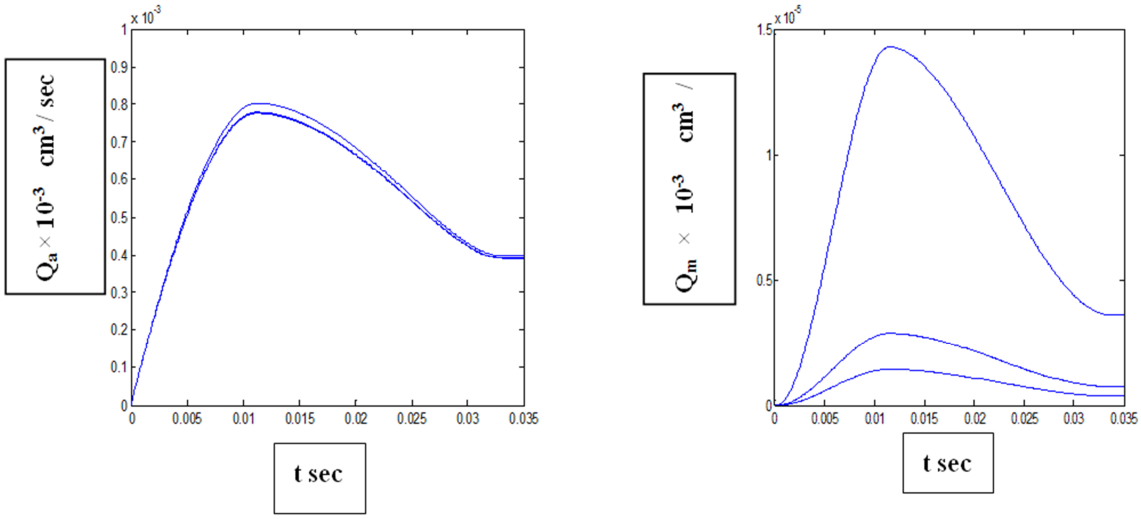

Fig. 4.1: Variation of Q_a and Q_m with t for different μ_s (ϕ_s =0.05 $gm^{-1}cm^2sec$, μ_m=5 poise)

Upper denotes μ_s = 0.01 poise

Middle denotes μ_s =0.05 poise

Lower denotes μ_s = 0.10 poise

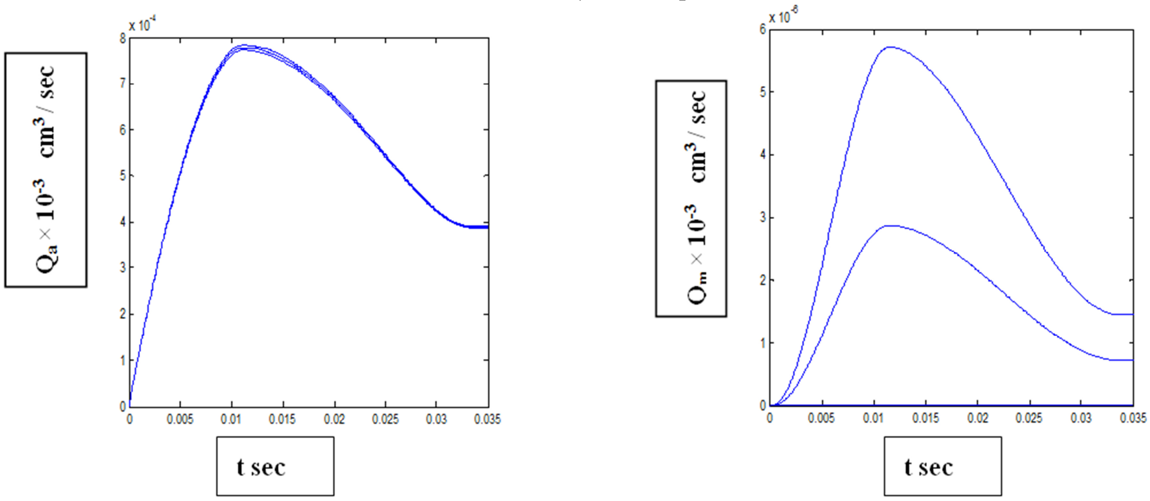

Fig. 4.2: Variation of Q_a , Q_m with t for different ϕ_s (μ_m = 5 poise, μ_s =0.05 poise)

Upper denotes ϕ_s =0.1 gm^{-1} cm^2 sec

Middle denotes ϕ_s =0.05 gm^{-1} cm^2 sec

Lower denotes ϕ_s =0 gm^{-1} cm^2 sec

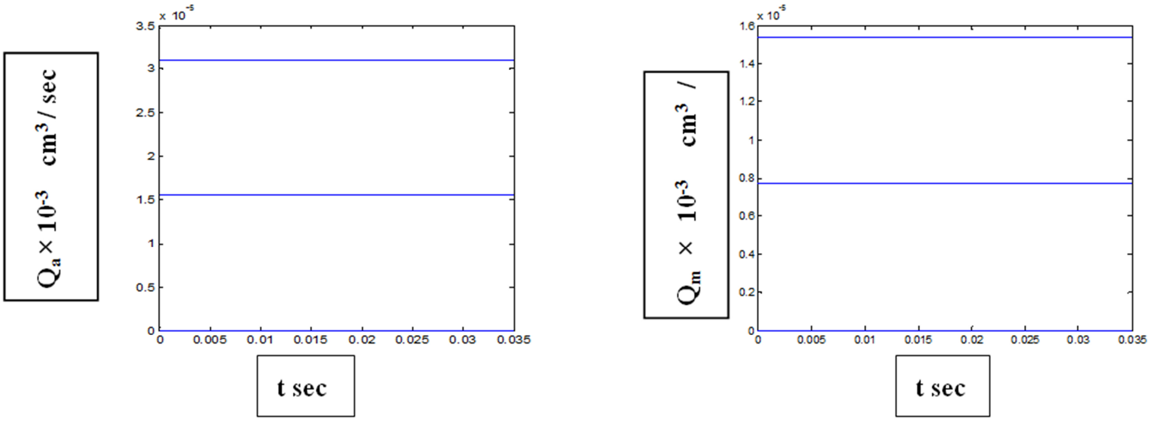

Fig. 4.3: Variation of Q_a and Q_m with t for different U_c (ϕ_s =0.05 gm^{-1} cm^2 sec, μ_s =0.05 poise, μ_m = 5 poise, P_0 = 0)

Upper denotes U_c= 0.1cm sec^{-1}
Middle denotes U_c =0.05 cm sec^{-1}
Lower denotes U_c = 0 cm sec^{-1}

5. Conclusions

From the analysis of the model the following results have been obtained.

1. Air and mucus flow rates follow the same pattern as the time dependent pressure gradient function representing Prolonged Mild Cough.
2. Air and mucus flow rates decrease with increase in serous fluid viscosity.
3. The effect of porosity of cilia bed and cilia beating has been found to increase the air and mucus flow rates.

It is pointed out here that these results are in agreement qualitatively with experimental results of various researches published in literature.

We hope that this study will throw some light on the role of cilia beating and serous fluid in mucus transport in the large airways due to prolonged mild cough.

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