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Roles of Airflow Velocity and Porosity Parameter on Mucus Transport in the Human Lung Airways under the Influence of Time Varying Pressure Gradient

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Abstract

This paper presents a two-layer circular unsteady state mathematical model and its analysis on mucus transport in the human lung airways. The model incorporates the roles of airflow velocity and porosity parameter on mucus transport under the influence of time varying pressure gradient generated due to coughing. The porosity parameter is incorporated because of immotile cilia forming a porous matrix bed in the serous sub-layer in contact with the epithelium in unhealthy state of human lung airways. The model also incorporates the effect of airflow velocity caused by high shear stress that shears secretions and unwanted foreign particles off the bronchial wall and propels them towards the larger airways and trachea under a normal cough mechanism. In the model, the mucus layer is taken as a visco-elastic fluid and the serous layer as an incompressible Newtonian fluid. The analysis of the model reveals that mucus transport rate increases with increase in airflow velocity, porosity parameter, acceleration due to gravity, mucus layer thickness and pressure gradient. It is also noted that the mucus transport rate decreases with the increase in coughing duration, mucus viscosity and its elastic modulus and viscosity of serous layer fluid.

Keywords: Mucus transport, immotile cilia, porosity, visco-elasticity.

Mathematics Subject Classification: 76A05, 76A10, 76D05, 76D10, 92B05,74F10

1. Introduction

The muco-ciliary system in the human lung airways is supposed to be made up of three layers; namely mucus layer, serous layer the cilia, which are tiny projections that resemble hairs and line the bronchial respiratory tract epithelium. Muco-ciliary clearance is one of the primary defense mechanism of the human lung airways. Under normal state, mucus and serous layer fluid are constantly swept from the upper respiratory tracts to the lower respiratory tracts of the human lung airways to remove mucus, but under the pathological state, the illness e.g. cystic fibrosis, chronic bronchitis, bronchial asthma, lung cancer, ciliary dyskinesia, etc. have negative impact on mucus transport in the human lung airways. The majority of these illnesses result in immotile cilia which form porous matrix bed. Immotile cilia and a lack of serous fluid are common in illnesses like cystic fibrosis. Since the mammalian bronchi are extremely sensitive, foreign particles like dust, straw, carcinogens, etc. or other sources of irritation like sneezing can cause airway contractions or the cough reflex, which releases mucus and air into the lung airways. Asthma, chronic bronchitis, and other pathological conditions are linked to coughing or cough reflex. The two main purposes of a normal cough in human beings are to help drive fluid discharges and other contaminants upward through the airways and to shield the lungs against aspiration[King et al.(1989)].

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Coughing is a natural mechanism that affects both healthy and unhealthy individuals. It is dependent on several aspects affecting several types of disorders, including cystic fibrosis, chronic bronchitis, and the asthama. Coughing facilitates the passage of secretions and other materials up through different airways, protecting the lungs against aspiration. Coughing ability to clear a specific airway depends on how quickly the gas descends the lumen. Since the tracheo-bronchial system is arranged so that each generation of bronchi has a gradually bigger total cross sectional area as it moves towards the alveoli, velocities for a given flow rate are lesser in narrower airways and greater in wider airways. Coughing is, therefore, expected to be more effective in clearing the larger airways than the smaller ones. Excessive mucus production is a result of respiratory conditions including cystic fibrosis and chronic bronchitis, and it is ejected through coughing or forced expiration. Coughing is the main defence mechanism for clearing mucus in situations of immotile cilia syndrome, which affects the airways.

Several investigators and researchers [Beavers and Joseph(1967),Pedley et.al (1970), Clarke (1973),Winet(1980),Puchelle (1983),David(2018),etc] have studied the mucus transport in the human lung airways in the last few decades. The cilium is viewed as an oscillating cylinder by Barton and Raynor (1967) who have studied an analytical model for mucus transport. The cilium is supposed to behave taller in length during the effective stroke and shorter during the recovery stroke. Specifically, compared to dry tubes [Clarke et al.(1970)] demonstrated a notable increase in airflow resistance in liquid-lined tubes at all flow speeds. It has been found that non-linear pressure-flow relationships in liquid-lined tubes under laminar flow conditions are caused by high-viscosity fluid occupying air space, which increases the flow resistance. Blake (1975) studied the two-layer Newtonian fluid model, which included one serous layer fluid and the other mucus layer. Blake also emphasised the significance of gravity and the impact of air movement on mucus transport.[Scherer and Burtz (1978)] hypothesised from a study carried out in vitro that the effect of coughing can extend to the seventeenth airway generation in conditions of excess mucus production that the complex relationship between the mucus viscosity, visco-elasticity, and surface tension determines how effective the cough is. Blake and Winet (1980) have also provided a mathematical study of the two-layer fluid model. They proposed that the mucus transport rate would be significantly increased if cilia could only pierce the upper, considerably more viscous layer. Coughing may not be particularly helpful to remove a very thin layer of mucus, thus the thickness of the mucus layer is also extremely significant. The existence of a sol phase at the bottom plate in the cough machine conducted by Zahm et al. (1989) has been shown to enhance mucus transport. They also looked at how coughing repeatedly affected the flow of mucus in a mock cough machine, and they found that the high shear rates during coughing significantly reduced the viscosity of the mucus.

A planar two-layer fluid model to explain muco-ciliary transport in the respiratory tract caused by cilia beating and air motion was well presented by King et al. (1993). They did this by treating mucus as a viscoelastic fluid and demonstrated that mucus transport rises with an increase in shear stress, pressure drop, acceleration due to gravity and mean velocity of cilia tips. It has been demonstrated that for given a fixed total thickness of serous layer fluid, the mucus transport rate will peak at a certain value of serous fluid thickness. A mathematical model of mucus transport in human lung airways have also been developed by Verma(1997), Verma and Tripathee (2013) and Verma and Rana (2015). They considered mucus as a visco-elastic fluid and accounts for air motion, cilia beating, and porosity parameter under steady-state circumstances. It has been demonstrated that the mucus transport rate falls with increasing serous and mucus layer viscosities and rises with air motion, cilia beating, and porosity parameter. By taking into account the impact of constriction on the airways, Kumar et al.(2016) examined mucus transport in sick airways. It has been demonstrated that when airway diameter rises, then mucus transport rate falls. By taking into account the effect of slip (porosity) parameter, Chitra and Shabana (2017) have proposed a two-layer model for the air-mucus interface in the constricted human lung airways under a time-varying pressure gradient. They have demonstrated that when the slip parameter rises, the mucus transport rate rises as well. In order to study mucus transport in human lung airways, Rana et al. (2021) have developed a two-layer circular steady-state mathematical model that takes into account the impacts of mucus visco-elasticity, cilia beating, and porosity parameter. By taking into account the porosity parameter, pressure gradient, and shear stress brought on by air-motion, Verma et al.(2021) have studied a two-layer planar unsteady state model for mucus transport in the human lung airways. It has been demonstrated that an increase in the porosity parameter, pressure gradient, and shear stress brought on by air motion contribute to an increase in the mucus transport rate.

Keeping all the above in view, a symmetrical two-layer unsteady state model for mucus transport in the human lung airways resulting from coughing is examined for low Reynolds number. The Dirac delta function is thought to capture the immediate pressure gradient that coughing creates in the fluid layers.

2. Mathematical Model

In human lung airways, the real situation of muco-ciliary system is idealised by the circular tube geometry represented by a symmetrical two-layer mathematical model as shown in Figure 1 with ciliated inner surface wall. It is assumed that the central lumen is filled with air and surrounded by visco-elastic mucus which is covered by a serous fluid with a viscosity significantly lower than that of the mucus.

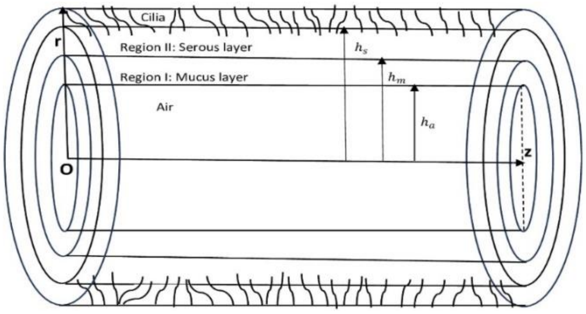

Figure 1: Schematic representation for mucus transport in human lung airways

This model accounts for the following factors in order to explore mucus transport in the human lung airways:

1. Mucus is assumed to be viscoelastic while serous layer is supposed to be an incompressible Newtonian fluid.
2. There are two sublayers of the serous layer fluid: one that is in contact with the epithelium and the other that is in contact with mucus. It is believed that cilia are immotile and create a porous matrix bed in the serous sub-layer, where flow may occur due to the porosity parameter and the pressure gradient [Beavers and Joseph (1967)]. In the serous sublayer in contact with the epithelium, no net flow is expected.
3. By imposing an airflow velocity as a boundary condition at the mucus-air interface, the influence of air motion is included.
4. The model also takes into account the effects of acceleration due to gravity and pressure gradient.

The transport equations for mucus and serous fluid under unsteady and low Reynolds number flow approximation are taken as follows:

Region-I, Mucus Layer ($h_a \le r \le h_m$)

$$\rho_m \frac{\partial u_m}{\partial t} = -\left(\frac{\partial p}{\partial z} - \rho_m g cos\theta\right) + \frac{1}{r}\frac{\partial}{\partial r}(r\tau_m) \tag{1}$$

$$\tau_m + \lambda \frac{\partial \tau_m}{\partial t} = \mu_m \frac{\partial u_m}{\partial r} \tag{2}$$

Region-II, Serous Layer($h_m \leq r \leq h_s$)

$$\rho_s \frac{\partial u_s}{\partial t} = -\left(\frac{\partial p}{\partial z} - \rho_s g cos\theta\right) + \frac{1}{r}\frac{\partial}{\partial r}\left(r\mu_s \frac{\partial u_s}{\partial r}\right) \tag{3}$$

where t is time and 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, θ is the angle by which the airway under consideration is inclined with the vertical.h_a, h_m and h_s are the thicknesses as 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 Figure 1.$\lambda(= \mu_m/G)$ is the relaxation time, G is the elastic modulus of mucus and τ_m is the shear stress in the mucus layer. Equation (2) represents the relation between the shear stress and shear rate for visco-elastic mucus.

The following conditions are taken for the system of equations (1)-(3):

Initial Conditions:

$$u_m = u_s = \tau_m = \frac{\partial \tau_m}{\partial t} = 0, \qquad t = 0 \tag{4}$$

Boundary Conditions:

$$u_m = U_a, \qquad r = h_a, \tag{5}$$

$$u_s = \beta \frac{\partial u_s}{\partial r}, \qquad r = h_s \tag{6}$$

Matching Conditions:

$$u_m = u_s = U_1, \qquad r = h_m \tag{7}$$

$$\tau_m = \mu_s \frac{\partial u_s}{\partial r}, \qquad r = h_m \tag{8}$$

where U_1 represents the mucus-serous sublayer interface velocity, which may be calculated by applying condition (8). At the mucus-serous sublayer interface, conditions (7) and (8) suggest that the velocities and stresses are continuous. U_a is the airflow velocity which incorporates the effect of airmotion. β is the porosity parameter incorporating the effects of immotile cilia.

3. Analytical Solution

Applying Laplace transform, the system of equations (1)-(3) becomes:

$$\frac{d^2\overline{U_m}}{dr^2} + \frac{1}{r}\frac{d\overline{U_m}}{dr} - k_m^2\overline{U_m} = 0 \tag{9}$$

$$\overline{\tau_m} = \frac{\mu_m}{1+\lambda S}\frac{d\overline{u_m}}{dr} \tag{10}$$

$$\frac{d^2\overline{U_s}}{dr^2} + \frac{1}{r}\frac{d\overline{U_s}}{dr} - k_s^2\overline{U_s} = 0 \tag{11}$$

Here, $\overline{U_m}$ and $\overline{U_s}$ are given by following relations:

$$S\rho_m\overline{u_m} - \overline{\phi_m} = \overline{U_m} \quad \text{and} \quad S\rho_s\overline{u_s} - \overline{\phi_s} = \overline{U_s}$$

where $k_m^2 = \frac{S\rho_m}{\mu_m}(1 + \lambda S) = \frac{S\rho_m}{G}(S + \alpha)$, $k_s^2 = \frac{S\rho_s}{\mu_s}$, $\alpha = \frac{G}{\mu_m}$, $\lambda = \frac{1}{\alpha}$,

$$\phi_m = -\left(\frac{\partial p}{\partial z} - \rho_m g cos\theta\right) \ and \ \phi_s = -\left(\frac{\partial p}{\partial z} - \rho_s g cos\theta\right)$$

In the above, S is the Laplace transform variable and bar $(-)$ denotes the Laplace transform of the corresponding function.

Using boundary and matching conditions (5)-(8) and solving equations (9)-(11), we have

$$\overline{u_m} = \frac{\overline{\phi_m}}{s\rho_m}\left[1 - \frac{\{K_0(k_m h_a) - K_0(k_m h_m)\}I_0(k_m r) + \{I_0(k_m h_m) - I_0(k_m h_a)\}K_0(k_m r)}{I_0(k_m h_m)K_0(k_m h_a) - I_0(k_m h_a)K_0(k_m h_m)}\right]$$
$$+\overline{U_a}\left[\frac{I_0(k_m h_m)K_0(k_m r) - K_0(k_m h_m)I_0(k_m r)}{I_0(k_m h_m)K_0(k_m h_a) - I_0(k_m h_a)K_0(k_m h_m)}\right]$$
$$+\overline{U_1}\left[\frac{K_0(k_m h_a)I_0(k_m r) - I_0(k_m h_a)K_0(k_m r)}{I_0(k_m h_m)K_0(k_m h_a) - I_0(k_m h_a)K_0(k_m h_m)}\right] \tag{12}$$

and

$$\overline{u_s} = \frac{\overline{\phi_s}}{s\rho_s}\left[1 - \frac{\{F_2 - K_0(k_s h_m)\}I_0(k_s r) + \{F_1 + I_0(k_s h_m)\}K_0(k_s r)}{F_1 K_0(k_s h_m) + F_2 I_0(k_s h_m)}\right]$$
$$+\overline{U_1}\left[\frac{F_2 I_0(k_s r) + F_1 K_0(k_s r)}{F_1 K_0(k_s h_m) + F_2 I_0(k_s h_m)}\right] \tag{13}$$

where $F_1 = \beta k_s I_1(k_s h_s) - I_0(k_s h_s)$, $F_2 = \beta k_s K_1(k_s h_s) + K_0(k_s h_s)$ and $\overline{U_1}$ is calculated by

$$\overline{U_1}\left[k_s\mu_s \frac{F_2 I_1(k_s h_m) - F_1 K_1(k_s h_m)}{F_1 K_0(k_s h_m) + F_2 I_0(k_s h_m)} + \frac{\mu_m k_m}{1+\lambda S}\left\{\frac{K_0(k_m h_a)I_1(k_m h_m) + I_0(k_m h_a)K_1(k_m h_m)}{I_0(k_m h_a)K_0(k_m h_m) - I_0(k_m h_m)K_0(k_m h_a)}\right\}\right]$$
$$= \frac{\overline{\phi_s}}{k_s}\left[\frac{\{F_2 - K_0(k_s h_m)\}I_1(k_s h_m) - \{F_1 + I_0(k_s h_m)\}K_1(k_s h_m)}{F_1 K_0(k_s h_m) + F_2 I_0(k_s h_m)}\right]$$
$$+\frac{\overline{\phi_m}}{k_m}\left[\frac{\{K_0(k_m h_a) - K_0(k_m h_m)\}I_1(k_m h_m) + \{I_0(k_m h_a) - I_0(k_m h_m)\}K_0(k_m h_m)}{I_0(k_m h_a)K_0(k_m h_m) - I_0(k_m h_m)K_0(k_m h_a)}\right]$$
$$+\frac{\overline{U_a}k_m\mu_m}{1+\lambda S}\left[\frac{I_0(k_m h_m)K_1(k_m h_m) + K_0(k_m h_m)I_1(k_m h_m)}{I_0(k_m h_a)K_0(k_m h_m) - I_0(k_m h_m)K_0(k_m h_a)}\right] \tag{14}$$

where I_0 and I_1 are modified Bessel functions of first kind and K_0 and K_1 are modified Bessel functions of second kind with order zero and unity respectively [Bowmann(1958)].

Now, the volumetric flow rates in the two layers are defined as follows:

$$\overline{Q_m} = \int_{h_a}^{h_m} 2\pi r\,\overline{u_m}dr \qquad \text{and} \qquad \overline{Q_m} = \int_{h_m}^{h_s} 2\pi r\,\overline{u_s}dr$$

Using equations (12)-(14), the expressions for flow rates become:

$$\overline{Q_m} = \frac{2\pi\overline{U_1}}{k_m}\left[\frac{\{h_m K_1(k_m h_m) - h_a K_1(k_m h_a)\}I_0(k_m h_a) + \{h_m I_1(k_m h_m) - h_a I_1(k_m h_a)\}K_0(k_m h_a)}{I_0(k_m h_m)K_0(k_m h_a) - I_0(k_m h_a)K_0(k_m h_m)}\right]$$
$$+\frac{2\pi\overline{U_a}}{k_m}\left[\frac{\{h_m K_1(k_m h_m) - h_a K_1(k_m h_a)\}I_0(k_m h_m) + \{h_m I_1(k_m h_m) - h_a I_1(k_m h_a)\}K_0(k_m h_m)}{I_0(k_m h_a)K_0(k_m h_m) - I_0(k_m h_m)K_0(k_m h_a)}\right]$$
$$+\frac{2\pi\overline{\phi_m}}{S\rho_m k_m}\left[\frac{\{h_m I_1(k_m h_m) - h_a I_1(k_m h_a)\}\{K_0(k_m h_a) - K_0(k_m h_m)\}}{I_0(k_m h_a)K_0(k_m h_m) - I_0(k_m h_m)K_0(k_m h_a)}\right]$$

$$+\frac{2\pi\overline{\phi_m}}{S\rho_m k_m}\left[\frac{\{h_m K_1(k_m h_m)-h_a K_1(k_m h_a)\}\{I_0(k_m h_a)-I_0(k_m h_m)\}}{I_0(k_m h_a)K_0(k_m h_m)-I_0(k_m h_m)K_0(k_m h_a)}\right]+\frac{\pi\overline{\phi_m}}{S\rho_m}(h_m^2-h_a^2) \quad (15)$$

and

$$\overline{Q_s}=\frac{2\pi\overline{U_1}}{k_s}\left[\frac{\{h_s I_1(k_s h_s)-h_m I_1(k_s h_m)\}F_2-\{h_s K_1(k_s h_s)-h_m K_1(k_s h_m)\}F_1}{F_1 K_0(k_s h_m)+I_0(k_s h_m)F_2}\right]$$

$$+\frac{2\pi\overline{\phi_s}}{S\rho_s k_s}\left[\frac{\{h_m I_1(k_s h_m)-h_s I_1(k_s h_s)\}\{F_2-K_0(k_s h_m)\}}{F_1 K_0(k_s h_m)+I_0(k_s h_m)F_2}\right]$$

$$+\frac{2\pi\overline{\phi_s}}{S\rho_s k_s}\left[\frac{\{h_s K_1(k_s h_s)-h_m K_1(k_s h_m)\}\{F_1+I_0(k_s h_m)\}}{F_1 K_0(k_s h_m)+I_0(k_s h_m)F_2}\right]+\frac{\pi\overline{\phi_s}}{S\rho_s}(h_s^2-h_m^2) \quad (16)$$

Now, approximating $\overline{\mathrm{Q_m}}$ and $\overline{Q_s}$ for larger values of arguments of Bessel functions, we get

$$\overline{Q_m}=\frac{2\pi}{k_m}\left(\overline{U_1}-\frac{\overline{\phi_m}}{S\rho_m}\right)\left[h_m coth\{k_m(h_m-h_a)\}-(h_a h_m)^{1/2}cosech\{k_m(h_m-h_a)\}\right]$$

$$+\frac{2\pi}{k_m}\left(\overline{U_a}-\frac{\overline{\phi_m}}{S\rho_m}\right)\left[h_a coth\{(h_m-h_a)k_m\}-(h_a h_m)^{1/2}cosech\{(h_m-h_a)k_m\}\right]$$

$$+\frac{\pi\overline{\phi_m}}{S\rho_m}(h_m^2-h_a^2) \quad (17)$$

and

$$\overline{Q_s}=\frac{2\pi}{k_s}\left(\overline{U_1}-\frac{\overline{\phi_s}}{S\rho_s}\right)\left[\frac{h_m coth\{k_s(h_s-h_m)\}-(h_s h_m)^{1/2}cosech\{k_s(h_s-h_m)\}}{1-\beta k_s coth[k_s(h_s-h_m)]}\right]$$

$$+\frac{2\pi\overline{\phi_s}}{k_s S\rho_s}\left[\frac{(h_s h_m)^{1/2}cosech\{k_s(h_s-h_m)\}-h_s coth\{k_s(h_s-h_m)\}-\beta k_s h_m}{1-\beta k_s coth[k_s(h_s-h_m)]}\right]$$

$$+\frac{\pi\overline{\phi_m}}{S\rho_m}(h_m^2-h_a^2) \quad (18)$$

where $\mathrm{U_1}$ is calculated by using the following relation:

$$\overline{U_1}\left[k_s\mu_s\frac{\beta k_s-coth[k_s(h_s-h_m)]}{1-\beta k_s coth[k_s(h_s-h_m)]}-\frac{k_m\mu_m}{(1+\lambda S)}coth[k_m(h_m-h_a)]\right]$$

$$=\frac{\overline{\phi_s}}{k_s}\left[\frac{(h_s/h_m)^{1/2}cosech[k_s(h_s-h_m)]-coth[k_s(h_s-h_m)]+\beta k_s h_m}{1-\beta k_s coth[k_s(h_s-h_m)]}\right]$$

$$+\frac{\overline{\phi_m}}{k_m}\left[(h_a/h_m)^{1/2}cosech[k_m(h_m-h_a)]-coth[k_m(h_m-h_a)]\right]$$

$$-\frac{\overline{U_a}k_m\mu_m}{1+\lambda S}\left[(h_a/h_m)^{1/2}cosech[k_m(h_m-h_a)]\right] \quad (19)$$

Although determining the accurate inverse Laplace transforms of $\overline{Q_m}$ and $\overline{Q_s}$ is difficult, the above expressions can be estimated by making appropriate assumptions such as thick mucus and thin serous layer fluid i.e. $\mathrm{k_m(h_m-h_a)} \gg 1$ and $\mathrm{k_s(h_s-h_m)} \ll 1$ respectively, then the expressions for $\overline{Q_m}$ and $\overline{Q_s}$ become:

$$\overline{Q_m} = 2\pi h_a \left[\frac{1}{S^{3/2}(S+\alpha)^{1/2}}\right]\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}} U_a + \frac{\pi}{\rho_m}\left[\frac{(h_m^2 - h_a^2)}{S} - \frac{2(h_m + h_a)}{S^{\frac{3}{2}}(S+\alpha)^{\frac{1}{2}}}\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}}\right]\phi_o e^{-st_o}$$

$$+\frac{2\pi}{\mu_s} h_m(h_s - h_m)\beta\left[\frac{(h_s - h_m - \beta)}{(S+\alpha)}\left(\frac{G}{\mu_s}\right) - \frac{1}{S^{\frac{1}{2}}(S+\alpha)^{\frac{1}{2}}}\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}}\right]\phi_o e^{-st_o}$$

$$+\frac{2\pi}{\rho_s} h_m^{\frac{1}{2}}\left(h_s^{\frac{1}{2}} - h_m^{\frac{1}{2}}\right)\left[\frac{(h_s - h_m - \beta)}{S(S+\alpha)}\left(\frac{G}{\mu_s}\right) - \frac{\beta(h_s - h_m)}{S^{\frac{1}{2}}(S+\alpha)^{\frac{1}{2}}}\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}}\left(\frac{\rho_s}{\mu_s}\right) - \frac{1}{S^{\frac{3}{2}}(S+\alpha)^{\frac{1}{2}}}\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}}\right]\phi_o e^{-st_o}$$

$$+\frac{2\pi}{\rho_m} h_m(h_s - h_m - \beta)\left[\frac{1}{S(S+\alpha)}\left(\frac{G}{\mu_s}\right) - \frac{(h_s - h_m - \beta)}{S^{\frac{1}{2}}(S+\alpha)^{\frac{3}{2}}}\frac{(G\rho_m)^{\frac{1}{2}}}{\mu_s^2} G + \frac{\beta(h_s - h_m)}{S+\alpha}\left(\frac{\rho_s}{\mu_s}\right)\left(\frac{G}{\mu_s}\right)\right]\phi_o e^{-st_o} \tag{20}$$

and

$$\overline{Q_s} = \frac{\pi}{\rho_s}\frac{(h_s^2 - h_m^2)}{S}\phi_o e^{-st_o} + \frac{2\pi}{\rho_s} h_m^{1/2}\left(h_m^{\frac{1}{2}} - h_s^{\frac{1}{2}}\right)\left[\frac{1}{S^{\frac{3}{2}}(S+\alpha)^{\frac{1}{2}}}\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}}\right]\phi_o e^{-st_o}$$

$$+\frac{2\pi\left(h_m^{\frac{1}{2}} - h_s^{\frac{1}{2}}\right)}{\rho_s(h_s - h_m - \beta)}\left[\frac{\beta(h_s - h_m)}{S^{\frac{1}{2}}(S+\alpha)^{\frac{1}{2}}}\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}}\left(\frac{\rho_s}{\mu_s}\right) - \frac{1}{S}\right]\phi_o e^{-st_o}$$

$$+\frac{2\pi}{\rho_s}\left(h_m^{\frac{1}{2}} - h_s^{\frac{1}{2}}\right)\left[\frac{\left(h_s^{\frac{1}{2}} - h_m^{\frac{1}{2}}\right)}{S^{\frac{3}{2}}(S+\alpha)^{\frac{1}{2}}}\left(\frac{\mu_s}{\rho_s}\right)(G\rho_m)^{\frac{1}{2}} + \frac{\beta(h_s - h_m)h_m^{\frac{1}{2}}}{S^{\frac{1}{2}}(S+\alpha)^{\frac{1}{2}}}\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}}\left(\frac{\rho_m}{\mu_s}\right) + \frac{1}{S(S+\alpha)}\left(\frac{G}{\mu_s}\right)\right]\phi_o e^{-st_o} \tag{21}$$

by using $\phi_m = \phi_s = \phi = \phi_o\delta(T), \delta(T)$ being Dirac delta function, where $T = t - t_o$. This is taken because of consideration of time varying pressure gradient taken in the proposed model.

Now, taking inverse Laplace transform of above, the values of Q_m and Q_s are given as follows:

$$Q_m = 2\pi\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}} h_a t e^{-\left(\frac{1}{2}\alpha t\right)}\left[I_o\left(\frac{\alpha t}{2}\right) + I_1\left(\frac{\alpha t}{2}\right)\right] U_a$$

$$+\frac{\pi}{\rho_m}\left[(h_m^2 - h_a^2) - 2\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}}(h_m + h_a)Te^{-\left(\frac{1}{2}\alpha T\right)}\left\{I_o\left(\frac{\alpha T}{2}\right) + I_1\left(\frac{\alpha T}{2}\right)\right\}\right]\phi_o u(T)$$

$$+\frac{2\pi}{\mu_s} h_m(h_s - h_m)\beta\left[H\left(\frac{G}{\mu_s}\right)e^{-(\alpha T)} - \left(\frac{G}{\rho_m}\right)^{\frac{1}{2}} e^{-\left(\frac{1}{2}\alpha T\right)} I_o\left(\frac{\alpha T}{2}\right)\right]\phi_o u(T)$$

$$+\frac{2\pi}{\rho_s} h_m^{\frac{1}{2}}\left(h_s^{\frac{1}{2}} - h_m^{\frac{1}{2}}\right)\left[H\left(\frac{\mu_m}{\mu_s}\right)\left(1 - e^{-(\alpha T)}\right) - \beta(h_s - h_m)\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}}\left(\frac{\rho_s}{\mu_s}\right)e^{-\left(\frac{1}{2}\alpha T\right)} I_o\left(\frac{\alpha T}{2}\right)\right.$$

$$\left. - \left(\frac{G}{\rho_m}\right)^{\frac{1}{2}} Te^{-\left(\frac{1}{2}\alpha T\right)}\left\{I_o\left(\frac{\alpha T}{2}\right) + I_1\left(\frac{\alpha T}{2}\right)\right\}\right]\phi_o u(T)$$

$$+\frac{2\pi}{\rho_m}h_m H\left[\left(\frac{\mu_m}{\mu_s}\right)\left(1-e^{-(\alpha T)}\right)+\beta(h_s-h_m)\left(\frac{\rho_s}{\mu_s}\right)\left(\frac{G}{\mu_s}\right)e^{-(\alpha T)}\right.$$
$$\left.-H\frac{(G\rho_m)^{\frac{1}{2}}}{\mu_s^2}GTe^{-\left(\frac{1}{2}\alpha T\right)}\left\{I_o\left(\frac{\alpha T}{2}\right)-I_1\left(\frac{\alpha T}{2}\right)\right\}\right]\phi_o u(T) \quad (22)$$

and

$$Q_s=\frac{\pi}{\rho_s}(h_s^2-h_m^2)\phi_o u(T)+\frac{2\pi}{\rho_s}h_m^{1/2}\left(h_m^{\frac{1}{2}}-h_s^{\frac{1}{2}}\right)\left[\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}}Te^{-\left(\frac{1}{2}\alpha T\right)}\left\{I_o\left(\frac{\alpha T}{2}\right)+I_1\left(\frac{\alpha T}{2}\right)\right\}\right]\phi_o u(T)$$
$$+\frac{2\pi\left(h_m^{\frac{1}{2}}-h_s^{\frac{1}{2}}\right)}{\rho_s H}\left[\beta(h_s-h_m)\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}}\left(\frac{\rho_s}{\mu_s}\right)e^{-\left(\frac{1}{2}\alpha T\right)}I_o\left(\frac{\alpha T}{2}\right)-1\right]\phi_o u(T)$$
$$+\frac{2\pi}{\rho_s}\left(h_m^{\frac{1}{2}}-h_s^{\frac{1}{2}}\right)\left[\left(h_s^{\frac{1}{2}}-h_m^{\frac{1}{2}}\right)\left(\frac{\mu_s}{\rho_s}\right)(G\rho_m)^{\frac{1}{2}}Te^{-\left(\frac{1}{2}\alpha T\right)}\left\{I_o\left(\frac{\alpha T}{2}\right)+I_1\left(\frac{\alpha T}{2}\right)\right\}\right.$$
$$\left.+\beta(h_s-h_m)h_m^{\frac{1}{2}}\left(\frac{G}{\rho_m}\right)^{\frac{1}{2}}\left(\frac{\rho_m}{\mu_s}\right)\left\{e^{-\left(\frac{1}{2}\alpha T\right)}I_o\left(\frac{\alpha T}{2}\right)\right\}+\left(\frac{G}{\mu_s}\right)\left(1-e^{-(\alpha T)}\right)\right]\phi_o u(T) \quad (23)$$

where $H=(h_s-h_m-\beta)$ and $u(T)$ is the unit step function.

4. Result and Discussion

To study the effect of various parameters on mucus transport rate quantitatively, expression for it given by equation (22), can be written in non-dimensional form as:

$$Q_m^*=2\pi\left(\frac{G^*}{\rho_m^*}\right)^{\frac{1}{2}}h_a^*t^*e^{-\left(\frac{1}{2}\alpha^*t^*\right)}\left[I_o\left(\frac{\alpha^*t^*}{2}\right)+I_1\left(\frac{\alpha^*t^*}{2}\right)\right]U_a^*$$
$$+\frac{\pi}{\rho_m^*}\left[(h_m^{*2}-h_a^{*2})-2(G^*\rho_m^*)^{\frac{1}{2}}(h_m^*+h_a^*)T^*e^{-\left(\frac{1}{2}\alpha^*T^*\right)}\left\{I_o\left(\frac{\alpha^*T^*}{2}\right)+I_1\left(\frac{\alpha^*T^*}{2}\right)\right\}\right]\phi_o^*u^*(T^*)$$
$$+\frac{2\pi}{\mu_s^*}h_m^*(1-h_m^*)\beta\left[H^*\left(\frac{G^*}{\mu_s^*}\right)e^{-(\alpha^*T^*)}-\left(\frac{G^*}{\rho_m^*}\right)^{\frac{1}{2}}e^{-\left(\frac{1}{2}\alpha^*T^*\right)}I_o\left(\frac{\alpha^*T^*}{2}\right)\right]\phi_o^*u^*(T^*)$$
$$+\frac{2\pi}{\rho_s^*}h_m^{*\frac{1}{2}}\left(1-h_m^{*\frac{1}{2}}\right)\left[H^*\left(\frac{\mu_m^*}{\mu_s^*}\right)\left(1-e^{-(\alpha^*T^*)}\right)-\beta^*(1-h_m^*)\left(\frac{G^*}{\rho_m^*}\right)^{\frac{1}{2}}\left(\frac{\rho_s^*}{\mu_s^*}\right)e^{-\left(\frac{1}{2}\alpha^*T^*\right)}I_o\left(\frac{\alpha^*T^*}{2}\right)\right.$$
$$\left.-\left(\frac{G^*}{\rho_m^*}\right)^{\frac{1}{2}}T^*e^{-\left(\frac{1}{2}\alpha^*T^*\right)}\left\{I_o\left(\frac{\alpha^*T^*}{2}\right)+I_1\left(\frac{\alpha^*T^*}{2}\right)\right\}\right]\phi_o^*U^*(T^*)$$
$$+\frac{2\pi}{\rho_m^*}h_m^*H^*\left[\left(\frac{\mu_m^*}{\mu_s^*}\right)\left(1-e^{-(\alpha^*T^*)}\right)+\beta^*(1-h_m^*)\left(\frac{\rho_s^*}{\mu_s^*}\right)\left(\frac{G^*}{\mu_s^*}\right)e^{-(\alpha^*T^*)}-\right.$$
$$\left.H^*\frac{(G^*\rho_m^*)^{\frac{1}{2}}}{\mu_s^{*2}}G^*T^*e^{-\left(\frac{1}{2}\alpha^*T^*\right)}\left\{I_o\left(\frac{\alpha^*T^*}{2}\right)-I_1\left(\frac{\alpha^*T^*}{2}\right)\right\}\right]\phi_o^*u^*(T^*) \quad (24)$$

by using the following set of non-dimensional parameters [King.et.al (1993), Agarwal and Verma (1997)]:

$$\mu_s^* = \frac{\mu_s}{\mu_o}, \quad \mu_m^* = \frac{\mu_m}{\mu_o}, \quad \rho_s^* = \frac{\rho_s}{\rho_o}, \quad \rho_m^* = \frac{\rho_m}{\rho_o}, \quad h_a^* = \frac{h_a}{h_s}, \quad h_m^* = \frac{h_m}{h_s}, \quad \alpha^* = \frac{G^*}{\mu_m^*},$$

$$G^* = \frac{\rho_o h_s^2}{\mu_o^2} G, \quad t^* = \frac{\mu_o}{\rho_o h_s^2} t, \quad t_o^* = \frac{\mu_o}{\rho_o h_s^2} t_o, \quad T^* = t^* - t_o^*, \quad \phi_o^* = \frac{LT}{\mu_o} \phi_o, \quad U_a^* = \frac{\rho_o L}{\mu_o} U_a,$$

$$\beta^* = \frac{\beta}{h_s}, \quad H^* = \frac{H}{h_s}, \quad Q_m^* = \frac{\rho_o L}{\mu_o h_s^2} Q$$

where μ_o and ρ_o are the viscosity and density of the serous sublayer fluid in contact with epithelium.

Various graphs are plotted for Q_m^* given by equation (24) in Figure (2) to (6) using the following set of parameters which have been calculated by using typical values of various characteristics related to air-ways [King et.al.(1993), Agarwal and Verma (1997)]:

$\mu_s^* = 1 - 4, \quad \mu_m^* = 100 - 1000, \quad \rho_s^* = 1, \quad \rho_m^* = 5, \quad h_a^* = 0.776, h_m^* = 0.820 - 0.830,$

$G^* = 15 - 30, t^* = (1.0 - 1.6) \times 10^{(-4)}, t_o^* = 0.4 \times 10^{(-4)}, \phi_o^* = 100 - 110, U_a^* = 1 - 8,$

$\beta^* = 0.01 - 0.04.$

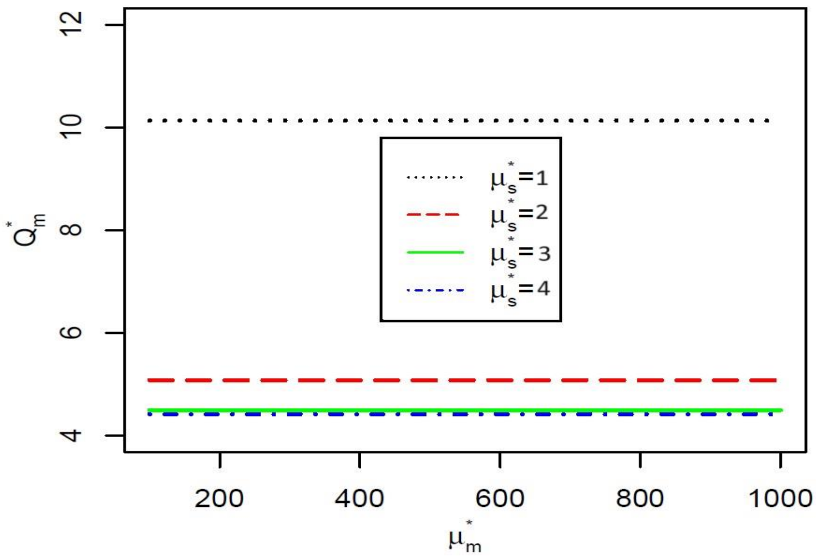

Figure 2: Variation of Q_m^* with μ_s^* for different values of μ_m^*

Figure 2 shows that for $\rho_s^* = 1, \rho_m^* = 5, h_a^* = 0.776, h_m^* = 0.826,\ G^* = 30, t^* = 1.0 \times 10^{-4}, t_o^* = 0.4 \times 10^{-4}, \phi_o^* = 100, U_a^* = 2, \beta^* = 0.01$,the mucus transport rate decreases with increasing serous layer fluid viscosity. This phenomenon is observed in cystic fibrosis patients, who have impaired mucus clearance and airway mucus obstruction. [David et al. (2018)]. This figure also shows that the mucus transport rate is not significantly affected by an increase in its viscosity. Furthermore, mucus from bronchitis patients has been shown to be more viscous during flare-ups of the condition [Samet and Cheng, (1994)]. For this reason, the results displayed in Figure 2 are consistent with the finding that mucus behaves like an elastic slab at higher values of mucus viscosity. [Ross and Corrsin (1974), King et al. (1985, 1989), Agarwal and Verma (1997), Verma (2010), Saxena and Tyagi (2015), Verma and Rana (2015), and Saxena et al. (2020)].

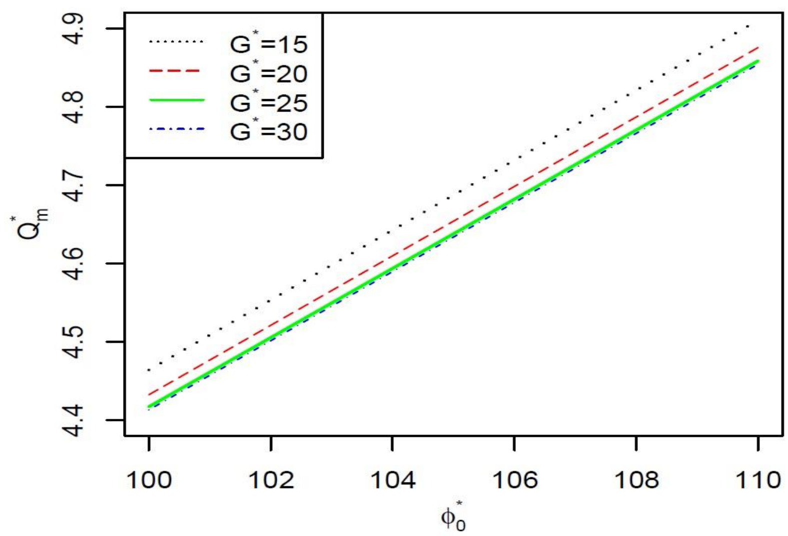

Figure 3: Variation of Q^*_m with ϕ^*_o for different values of G^*

Figure 3 illustrates that for $\rho^*_s = 1, \rho^*_m = 5, h^*_a = 0.776, h^*_m = 0.826, \mu^*_m = 1000,\ \mu^*_s = 3, t^* = 1.0 \times 10^{-4}, t^*_o = 0.4 \times 10^{-4}, U^*_a = 2, \beta^* = 0.01$, the mucus transport rate increases with increasing pressure drop and acceleration due to gravity and decreases with increasing mucus elastic modulus.This outcome agrees with the conclusions made in their mathematical models given by King et al. (1993) and Agarwal and Verma (1997).

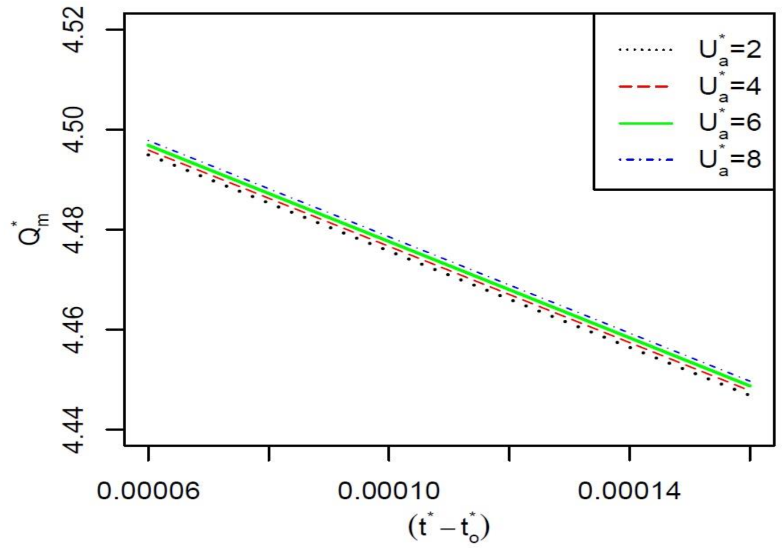

Figure 4: Variation of Q^*_m with $t^* - t^*_o$ for different values of U^*_a

Figure 4 illustrates that for $\rho^*_s = 1, \rho^*_m = 5, h^*_a = 0.776, h^*_m = 0.826, \mu^*_m = 1000, \mu^*_s = 3, \phi^*_o = 100, G^* = 30, \beta^* = 0.01$,the mucus transport rate decreases with an increase in coughing duration and increases as the airflow velocity at the mucus-air interface increases.The former result is consistent with a study by King et al. (1985) that used the rigid tube model to extend cough duration by increasing up-stream resistance, which decreased peak flow rate and, in turn, decreased cough effectiveness.

Figure 5 shows that for $\rho^*_s = 1, \rho^*_m = 5, h^*_a = 0.776, t^* = 1.0 \times 10^{-4}, t^*_o = 0.4 \times 10^{-4}, \mu^*_m = 1000, \mu^*_s = 3, \phi^*_o = 100, U^*_a = 2, \beta^* = 0.01$,the mucus transport rate increases with increasing mucus layer thickness and decreases with increasing mucus elastic modulus. It is should be mentioned that the outcome is consistent with the results of Clark et al. (1970), who reported better mucus-airflow interaction with reduced viscosity and greater mucus layer thickness.

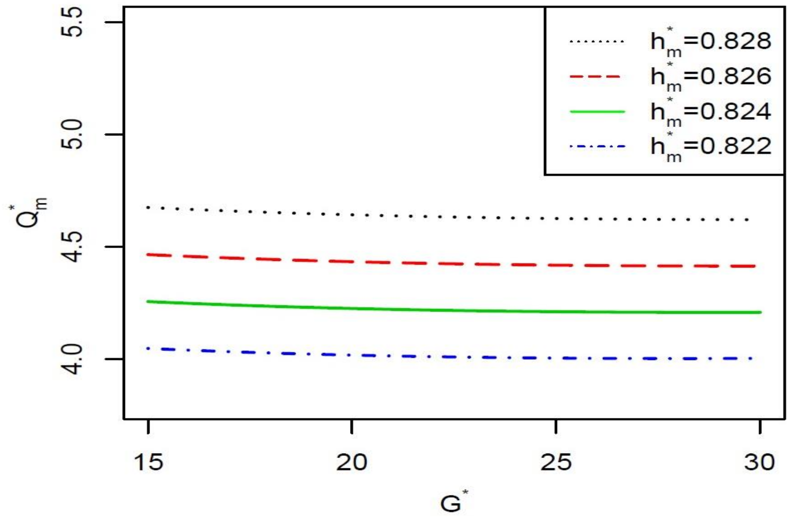

Figure 5: Variation of Q_m^* with G^* for different values of h_m^*

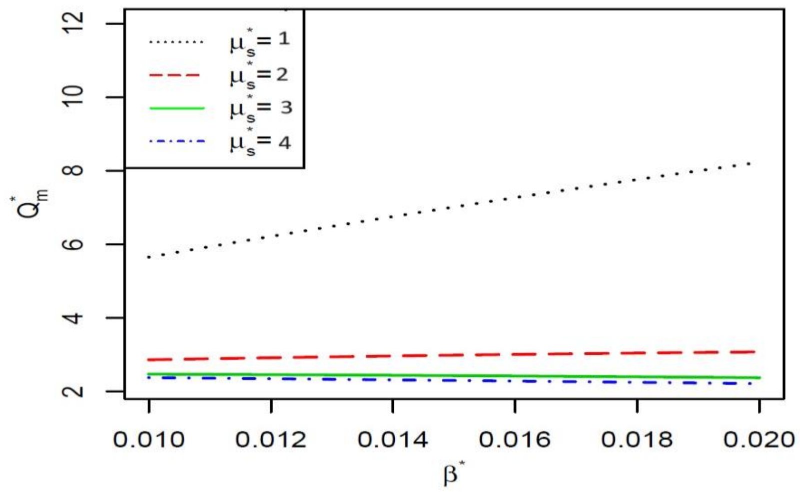

Figure 6: Variation of Q_m^* with β^* for different values of μ_s^*

From Figure 6, it is noted that for $\rho_s^* = 1, \rho_m^* = 5, h_a^* = 0.776, h_m = 0.826, t^* = 1.0 \times 10^{-4}, t_o^* = 0.4 \times 10^{-4}, \mu_m^* = 1000, \phi_o^* = 100, U_a^* = 2, G^* = 30$, the mucus transport rate increases with increasing porosity parameter but decreases with increasing viscosity of the serous fluid. These findings correlate with the findings of Agarwal and Verma (1997), Verma (2010), Saxena and Tyagi (2015), Verma and Rana (2015), and Rana et al.(2021).

From Figure 7, it is seen that for $\rho_s^* = 1, \rho_m^* = 5, h_a^* = 0.776, t^* = 1.0 \times 10^{-4}, t_o^* = 0.4 \times 10^{-4}, \mu_m^* = 1000, G^* = 30, \phi_o^* = 100, U_a^* = 2, \beta^* = 0.01$, the mucus transport rate increases with an increase in mucus layer thickness. Also, it is observed that when mucus viscosity increases, then its transport rate decreases.

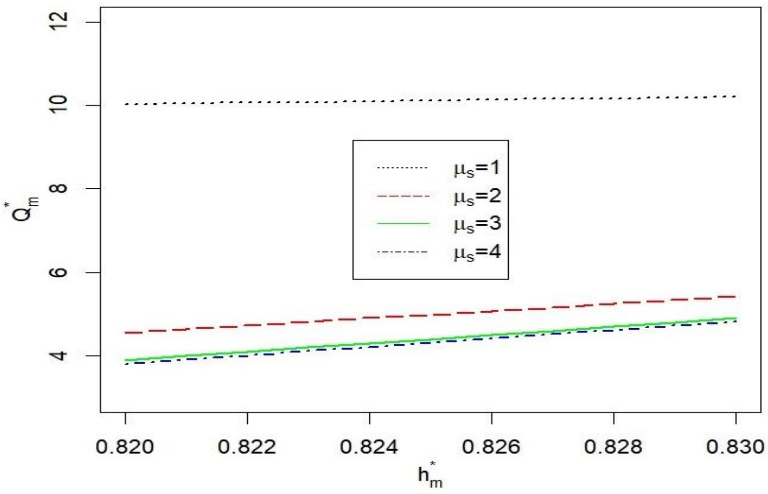

Figure 7: Variation of Q_m^* with h_m^* for different values of μ_s^*

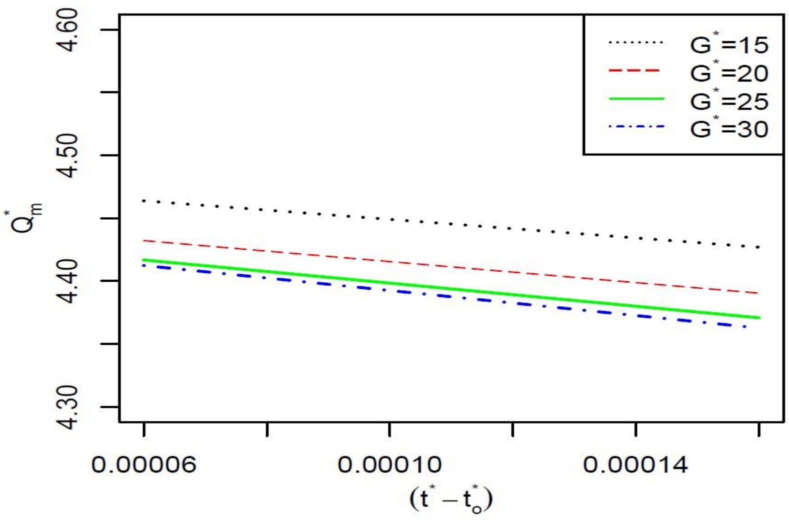

Figure 8: Variation of Q_m^* with $t^* - t_o^*$ for different values of G^*

Figure 8 illustrates that for $\rho_s^* = 1, \rho_m^* = 5, h_a^* = 0.776, h_m^* = 0.826, \mu_m^* = 1000, \mu_s^* = 3, \phi_o^* = 100, U_a^* = 2, \beta^* = 0.01$, the mucus transport rate decreases with increase in cough duration and elastic modulus of mucus.

5. Conclusion

The results of this study indicate that the mucus transport rate increases when airflow velocity increases because of high shear stress. It also increases when the mucus layer thickness, porosity parameter because of immotile cilia, pressure drop in the fluid layers, and acceleration due to gravity increase. It also finds that an increase in mucus viscosity, serous fluid viscosity, mucus elastic modulus and cough duration results in a decrease in mucus transport rate.

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