Original article:

Four Layer Cylindrical Model of Mucus Transport in the Lung: Effect of Prolonged Cough

Arti Saxena[1], Vijay Kumar[2], J. B. Shukla[3]

Abstract:

Background: In this paper, a four layer model of the simultaneous and coaxial flow of moist air, mucus, mixture of mucin and periciliary liquid and serous fluid (assumed to be incompressible and Newtonian fluids) in a circular tube under time dependent pressure gradient representing prolonged cough is analyzed to study the mucus transport in an airway in the presence of prolonged cough. It is assumed that air and mucus flow under quasi steady state turbulent conditions while the mixture of mucin and periciliary liquid and serous layer surrounding mixture layer flows under unsteady laminar condition in presence of immotile cilia carpet. ***Result:*** It is shown that the mucus transport increases as the viscosity of serous fluid decreases. Also the mixture and serous fluid flow rates increase as the viscosity of serous fluid decreases. It is also observed that the effect of resistance to flow by serous fluid in the cilia bed is to decrease flow rates. The flow rates of mucus and mixture of mucin and periciliary fluid increase as the viscosity of mixture decreases also air and mixture of mucus and periciliary fluid flow rates increase as the thickness of mixture increases. ***Conclusion:*** As the thickness of mucus increases its flow rate increases on the other hand the mixture flow rate, mucus and serous fluid flow rate decreases with the increase of the mixture thickness.

Keywords: Mucus Transport; Cylindrical Model; Prolonged Cough; Newtonian fluid.

Bangladesh Journal of Medical Science Vol. 19 No. 01 January'20. Page : 53-63
DOI: https://doi.org/10.3329/bjms.v19i1.43873

Introduction

Under pathological conditions of the lung, various diseases such as chronic bronchitis, cystic fibrosis, etc. excessive mucus is formed and is transported by forced expiration or cough[1,2,3]. In other way around, when airways are affected by immotile cilia syndrome (dyskinesia), cough is the main mechanism by which mucus is transported. In recent decades, several experiments related to two phase flow in tubes under externally applied pressure have been studied to simulate mucus transport in airways due to cough [4-6, 7, 8, 9]. In particular, Clarke[4] has shown that the resistance to air flow through a liquid lined tube is markedly increased at all flow rates in comparison to the case of a dry tube. They noticed that at all flow rates compatible with laminar flow conditions the pressure flow relationship in liquid lined tube is nonlinear and the resistance to flow being greater than that the expected from narrowing alone. Under dry tube condition, this result is expected to be high, as viscous fluid occupies the corresponding air-space. Further, they have pointed out that, after the onset of turbulence there is a considerable increase in flow resistance which occurs simultaneously with wave formation on the surface of liquid film. These effects are more marked with respect to thicker liquid with low viscosity. Scherer and Burtz[8] and Scherer[3] have conducted fluid mechanical experiments relevant to cough, using air and liquid blown out of a straight tube by turbulent air jet. Kim[7] have studied mucus transport in vertical tubes by two phase (gas, liquid) flow mechanism and noted that the elasticity of mucus does not affect its transport.

Renowned researchers conducted several other experimental investigations in a cough machine (a parallel plate channel) under turbulent flow condition by simulating mucus transport in the trachea due to cough[10, 11, 1, 2, 12, 13]. In particular, King [13] in their

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experiments found no apparent relationship between elasticity of mucus and its transport. Zahm[10] in their experimental studies in a cough machine pointed out that mucus transport increases due to the presence of a sol phase at bottom plate. Agarwal[11] have studied the mucus gel transport in a constricted simulated cough machine and found that mucus transport increases in presence of serous fluid. Agarwal[23] have also studied by means of experiment, the transport of mucus gel in a simulated cough machine where the bottom plate was grooved and, flooded with serous fluid and found that the mucus transport increases as the cross-sectional area formed by grooves saturated with serous fluid increases. Thus, he suggested the importance of topography and slipperiness of the bottom surface. In this paper, we study the simultaneous flow of air and mucus in a pipe simulating mucus transport in airways due to cough under the certain assumptions as given in[3, 8-9, 14-17].

The mixture of mucin and periciliary layer in contact with cilia bed flows very slowly[18] i.e. laminar as the corresponding Reynold number is very small, and flows under unsteady state condition caused by time dependent pressure gradient representing cough. Also, the serous fluid flow rate is assumed to be generalized unsteady laminar governed by Darcy's Law.

By considering all these facts and assumptions and using Prandtl mixing length theory[19], the means of quasi-steady and unsteady state equations in the turbulent and laminar layers can be written in cylindrical coordinates.

MATHEMATICAL MODEL:

Region I: Air flow under Quasi steady turbulent conditions $\left(0 \le r \le R_a\right)$:

$$-\frac{\partial p}{\partial z}+\frac{1}{r}\frac{\partial}{\partial r}\left(r\tau_a\right)=0 \qquad (2.1)$$

$$\tau_a=\rho_a l_a^2\left|\frac{\partial u_a}{\partial r}\right|\frac{\partial u_a}{\partial r}=-\rho_a l_a^2\left(-\frac{\partial u_a}{\partial r}\right)^2 \qquad (2.2)$$

Region II: Mucus Flow under Quasi steady turbulent conditions $\left(R_a \le r \le R_m\right)$:

$$-\frac{\partial p}{\partial z}+\frac{1}{r}\frac{\partial}{\partial r}\left(r\tau_m\right)=0 \qquad (2.3)$$

$$\tau_m=\rho_m l_m^2\left|\frac{\partial u_m}{\partial r}\right|\frac{\partial u_m}{\partial r}=-\rho_m l_m^2\left(-\frac{\partial u_m}{\partial r}\right)^2 \qquad (2.4)$$

Region III: Unsteady laminar flow of mixture of mucin and periciliary liquid $\left(R_m \le r \le R_s\right)$:

$$-\frac{\partial p}{\partial z}+\frac{1}{r}\frac{\partial}{\partial r}\left(r\tau_{ms}\right)=\rho_{ms}\frac{\partial u_{ms}}{\partial t} \qquad (2.5)$$

$$\tau_{ms}=\mu_{ms}\frac{\partial}{\partial r}\left(u_{ms}\right) \qquad (2.6)$$

Region IV: Unsteady laminar flow of serous fluid in the cilia bed forming a porous matrix $\left(R_s \le r \le R\right)$:

$$-\frac{\partial p}{\partial z}-\frac{\mu_s}{\phi_s}u_s=\rho_s\frac{\partial u_s}{\partial t} \qquad (2.7)$$

In equation (2.1) - (2.7), the notations are as:

where, t : time;

z : coordinate along the flow direction also the axis of the tube;

r : coordinate perpendicular to fluid flow in the radial direction;

R_a : airway thickness;

R : radius of tube;

P : the mean pressure which is constant across three layers;

u_a, u_m, u_s : mean velocity components of air, mucus and serous fluid ;

u_{ms} :velocity component of mixture of mucin and periciliary liquid in the z direction;

τ_a : mean shear stress in the air;

τ_m : mean shear stress in the turbulent mucus layer;

τ_{ms} : mean shear stress in the laminar mixture layer;

ρ_a, ρ_m and ρ_s are the densities of air, mucus and serous fluid respectively;

μ_s : viscosity of serous fluid and

μ_{ms} : viscosity of mixture.

The mixing lengths l_a, l_m, l_{ms} are assumed as follows:

$$l_a=l_0\left(R-r\right) \qquad (2.8)$$

$$l_m=l_1\left(R-r\right) \qquad (2.9)$$

where: l_0, l_1 are constants and determined experimentally.

INITIAL CONDITION

$u_s=0, u_{ms}=0$ at $t=0$ (2.10)

BOUNDARY CONDITION

$\frac{\partial u_a}{\partial r}=0$ at $r=0$ (2.11)

MATCHING CONDITIONS

$u_a=u_m,\quad \tau_a=\tau_m$ at $r=R_a$ (2.12)

$u_m=u_{ms},\quad \tau_m=\tau_{ms}$ at $r: R_m$

(2.13)

$u_{ms} = u_s$ at $r = R_s$ (2.14)

Equations (2.12) - (2.14) represent the continuity of the velocity and stress components at the two interfaces. During prolonged cough, the pressure gradient generated in the lung is time dependent[22].

We assume that

$$-\frac{\partial p}{\partial z} = P = P_0 f(t) \quad (2.15)$$

where, P_0 is a constant and its magnitude is proportionate to the cough intensity. It can be seen clearly that as it increases the flow rates also increase proportionally.

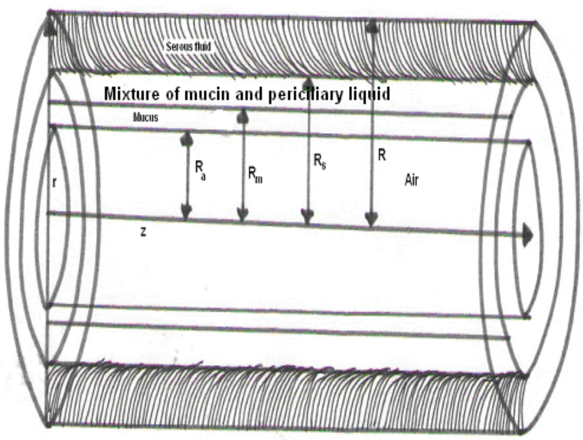

Fig:2.1: Mucus Transport in a circular tube

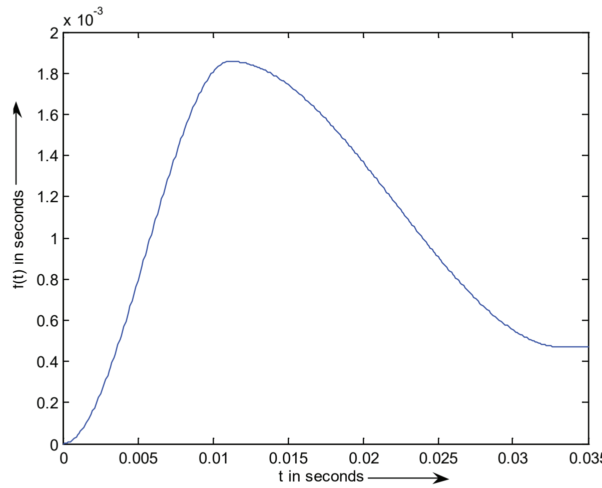

Fig 2.2: Graphical presentation of the function

The function $f(t)$ in (2.15) represents the prolonged mild cough and is given by,

$$f(t) = \begin{cases} \frac{321\, t^2}{640\, T_m}\left(1 - \frac{2t}{3T_m}\right), & 0 \le t \le T_m \\ \frac{9}{32} t \left(1 - \frac{9t}{10T}\right)^2 + \frac{T}{64}, & T_m \le t \le \frac{T}{\alpha} \\ \frac{T}{64}, & t \ge \frac{T}{\alpha} \end{cases} \quad (2.16)$$

Where, T is the cough duration, $\alpha = 0.9$ and $T_m = 0.011$ sec.

Discussion and results

To see the effect of various parameters on flow rates Q_a, Q_m, Q_{ms} and Q_s we have drawn different graphs using MATLAB. We have varied the thickness of mucus layer and mixture in such a way that the radial thickness of the turbulent mucus zone increases and the corresponding air layer thickness decreases. Similarly to see the effect of thickness of layer of mixture on serous fluid flow rate we have varied R_s keeping R_m fixed so that as thickness of mixture increases, serous fluid thickness decreases. To study these aspects we have drawn the graphs of Q_a, Q_m, Q_{ms} and Q_s with respect to $(R_m - R_a)$ and $(R_s - R_m)$ for fixed values of viscosity and porosity coefficient.

Here we are considering the second generation (larger airways) i.e. R = 46.45 × 10^{-2} cm. To analyze air flow rate and mucus transport quantitatively, the expressions for Q_a, Q_m, Q_{ms} and Q_s have been calculated and plotted under the following set of parameters [14-15, 21].

T = .03sec, t =0-0.08 sec, P_0 = 1.00 × 10^5 gm cm^{-2} sec^{-2}, $l_0 = l_1$ = 0.40, R_a = 31.45×10^{-2} cm, R_m = 38.45×10^{-2} cm, R_s = 40.45×10^{-2}cm, ρ_{ms} = 0.2-0.8 gm cm^{-3}, ρ_s = 0.1-0.6 gm cm^{-3}, ρ_a = 1.00 × 10^{-3} gm cm^{-3}, μ_s = 1.00-10.00 × 10^{-2} poise, ρ_m = 1.00 gm cm^{-3}, ϕ_s = 0.01-0.10 gm^{-1} cm^2 sec

Figure 4.1 and 4.2 illustrate the effect of pressure gradient on air, mucus, mixture of mucus

SOLUTION OF MODEL

To see the effect of resistance to flow by serous fluid in the cilia bed we solve the model (2.1)-(2.7) by using the boundary condition (2.11) and the matching conditions given by (2.12) -(2.14).

In each layer the volumetric flow rates can be defined as:

$$Q_a = \int_0^{R_a} 2\pi r\, u_a\, dr \;;\; Q_m = \int_{R_a}^{R_m} 2\pi r\, u_m\, dr\,;\, Q_{ms} = \int_{R_m}^{R_s} 2\pi r\, u_{ms}\, dr\,;\, Q_s = \int_{R_s}^{R} 2\pi r\, u_s\, dr \tag{3.1}$$

which after using velocity components can be written as follows:

$$\frac{Q_a}{2\pi} = \frac{\varphi_s R_a^2 P}{2\mu_s}\left[1 - e^{-\frac{\mu_s}{\rho_s \varphi_s}t}\right] + \frac{PR_a^2}{8\mu_{ms}}\left(R_s^2 - R_m^2\right) - \frac{\rho_{ms}\psi_{ms}R_a^2}{4\mu_{ms}}\left(\frac{R_s^2 - R_m^2}{2} + R_m^2 \ln\frac{R_m}{R_s}\right)$$
$$+\frac{R^2}{2l_0}\left(\frac{PR}{2\rho_a}\right)^{\frac{1}{2}}\left[\ln\left(\frac{R^{\frac{1}{2}} + R_a^{\frac{1}{2}}}{R^{\frac{1}{2}} - R_a^{\frac{1}{2}}}\right) - 2\left(\frac{R_a}{R}\right)^{\frac{1}{2}}\left\{1 + \frac{R_a}{3R} + \frac{R_a^2}{5R^2}\right\}\right] + \frac{R_a^2}{2l_1}\left(\frac{2PR}{\rho_m}\right)^{\frac{1}{2}}\left[\ln\left(\frac{R^{\frac{1}{2}} + R_m^{\frac{1}{2}}}{R^{\frac{1}{2}} + R_a^{\frac{1}{2}}}\right) - \frac{1}{2}\ln\left(\frac{R - R_m}{R - R_a}\right) - \frac{R_m^{\frac{1}{2}} - R_a^{\frac{1}{2}}}{R^{\frac{1}{2}}}\right]$$

(3.2)

$$\frac{Q_m}{2\pi} = \frac{\varphi_s P}{2\mu_s}\left[1 - e^{-\frac{\mu_s}{\rho_s \varphi_s}t}\right]\left[R_m^2 - R_a^2\right] + \frac{P}{8\mu_{ms}}\left(R_s^2 - R_m^2\right)\left(R_m^2 - R_a^2\right) - \frac{\rho_{ms}\psi_{ms}\left(R_m^2 - R_a^2\right)}{4\mu_{ms}}\left(\frac{R_s^2 - R_m^2}{2} + R_m^2 \ln\left(\frac{R_m}{R_s}\right)\right)$$
$$+\frac{1}{l_1}\left(\frac{PR}{2\rho_m}\right)^{\frac{1}{2}}\left[\frac{R^2 - R_a^2}{2}\left\{\ln\left(\frac{R^{\frac{1}{2}} + R_m^{\frac{1}{2}}}{R^{\frac{1}{2}} - R_m^{\frac{1}{2}}}\right) - \ln\left(\frac{R^{\frac{1}{2}} + R_a^{\frac{1}{2}}}{R^{\frac{1}{2}} - R_a^{\frac{1}{2}}}\right)\right\} + \left(\frac{R_a}{R}\right)^{\frac{1}{2}}\left(\frac{15R^2 + 5R_a R - 12R_a^2}{15}\right) - \left(\frac{R_m}{R}\right)^{\frac{1}{2}}\left(\frac{15R^2 + 5R_m R + 3R_m^2 - 15R_a^2}{15}\right)\right]$$

(3.3)

$$\frac{Q_{ms}}{2\pi} = \frac{\phi_s P\left(R_s^2 - R_m^2\right)}{2\mu_s}\left[1 - e^{-\frac{\mu_s}{\rho_s \phi_s}t}\right] + \frac{P}{\mu_{ms}}\left(\frac{\left(R_s^2 - R_m^2\right)}{4}\right)^2 - \frac{\rho_{ms}\psi_{ms}}{4\mu_{ms}}\left(\frac{\left(R_s^2 - R_m^2\right)\left(R_s^2 - 3R_m^2\right)}{4} - R_m^4 \ln\frac{R_m}{R_s}\right) \quad 3.4)$$

$$\frac{Q_s}{2\pi} = \frac{\phi_s P}{2\mu_s}\left[R^2 - R_s^2\right]\left[1 - e^{-\frac{\mu_s}{\rho_s \phi_s}t}\right] \tag{3.5}$$

Averaging method by Sestak and Charles[20] has been used for solving the unsteady equations in laminar layer and thus, by substituting the acceleration term on the right hand side of equations (2.5) by its mean value across the thickness i.e.

$$\frac{\partial u_{ms}}{\partial t} \approx \Psi_{ms} = \frac{1}{R_s - R_m}\int_{R_m}^{R_s} \frac{\partial u_{ms}}{\partial t}\, dr \tag{3.6}$$

then equation (2.5) reduces to

$$\frac{\partial}{\partial r}\left(r\tau_{ms}\right) = -\left(P - \rho_{ms}\Psi_{ms}\right) r \tag{3.7}$$

Where Ψ_m is a time dependent function, and *P* as given in equation (2.15).

To determine ψ_m we differentiate Equation (3.1.6) with respect to t to get

$$\frac{\partial u_{ms}}{\partial t} = \frac{P'\phi_s}{\mu_s}\left(1 - e^{-\frac{\mu_s}{\rho_s \phi_s}t}\right) + \frac{P}{\rho_s}e^{-\frac{\mu_s}{\rho_s \phi_s}t} + \left(\frac{R_s^2 - r^2}{4\mu_{ms}}\right)P' - \frac{\rho_{ms}\psi'_{ms}}{2\mu_{ms}}\left[\frac{R_s^2 - r^2}{2} + R_m^2 \ln\frac{r}{R_s}\right] \tag{3.8}$$

where (') denotes the derivative with respect to t.

Now on solving (3.1.13) using (3.1.15) we get,

$$\psi'_{ms} + \frac{\psi_{ms}}{a_2} = P'\frac{a_1}{a_2} + \frac{1}{a_2}e^{-\frac{\mu_s}{\rho_s \phi_s}t}\left(\frac{P}{\rho_s} - P'\frac{\phi_s}{\mu_s}\right) \tag{3.9}$$

Where,

$$a_1 = \left[\frac{\left(2R_s + R_m\right)\left(R_s - R_m\right)}{12\mu_{ms}} + \frac{\phi_s}{\mu_s}\right] \; and \; a_2 = \frac{\rho_{ms}}{2}\left[\frac{\left(2R_s + R_m\right)\left(R_s - R_m\right)}{6\mu_{ms}} - \frac{R_m^2}{\mu_{ms}}\left(1 + \frac{R_m}{R_s - R_m}\ln\frac{R_m}{R_s}\right)\right]$$

On solving (3.9) using (2.15) and (2.16) we will get ψ_{ms}

Ethical clearance: This study was approved ethically by the local ethics committee.

andpericiliary liquid and serous fluid flow rates for ϕ_s =0.05 gm^{-1} cm^2 sec and various values of viscosities of serous fluid and mixture of mucin and periciliary liquid and so the observation is that these flow rates increase as the serous fluid viscosity or the viscosity of mixture decreases but there is a very negligible effect on air flow. Also the viscosity of mixture does not effect the serous fluid flow rate. Figure 4.3 illustrates the effect of porosity of serous fluid in the cilia bed. It can be seen clearly from these figures that porosity tends to increase the flow rates for fixed μ_s = 0.05 poise and μ_{ms} = 0.5 poise. Figure 4.4 illustrates the effect of the thickness of mucus layer for fixed R and R_m and from these figures it can be seen that for fixed values of μ_s and ϕ_s, the flow rate of mucus increases with its thickness [Figure 4.4a] whereas flow rate of air decreases and there is a no effect on mixture and serous fluid flow rates[Figure 4.4b]. Figure 4.5 illustrates the effect of thickness of mixture of mucus and periciliary liquid for fixed R, (R_m -R_a) and from these figures it can be seen that for fixed values of μ_s and ϕ_s, the flow rates of air and mixture increase as we increase the thickness of mixture [Figure 4.5a] whereas mucus and serous fluid flow rates decreases [Figure 4.5b].

Conclusions

In this paper, we have studied air and mucus flow under prolonged cough conditions by representing it as a circular tube. The prolonged cough has been represented by a time dependent pressure gradient function. The simultaneous and coaxial flow of air, mucus in a tube are considered to flow under quasi steady turbulent conditions and mixture of mucin and periciliary fluid is considered to flow under unsteady laminar condition and serous fluid surrounding the mixture layer coaxially is also assumed to flow under unsteady laminar condition.

The conclusions of our model analysis are as follows:

1. It is observed that mucus transport increases as the viscosity of serous fluid decreases. Also the mixture and serous fluid flow rates increase as the viscosity of serous fluid decreases.
2. It has been shown that the effect of resistance to flow by serous fluid in the cilia bed is to decrease flow rates.
3. The flow rates of mucus and mixture of mucin and periciliary fluid increase as the viscosity of mixture decreases.
4. Air and mixture of mucus and periciliary fluid flow rates increase as the thickness of mixture increases.
5. As the thickness of Mucus increases its flow rate increases on the other hand the mixture flow rate decreases.
6. Mucus and Serous fluid flow rate decreases as mixture thickness increases.

Conflict of interest:

The author(s) declared no potential conflicts of interest.

Individual Contribution of the Authors:

Conceptual work: Arti Saxena, Vijay Kumar, J. B. Shukla

Data collection: Arti Saxena, Vijay Kumar, J. B. Shukla

Manuscript writing: Arti Saxena, Vijay Kumar, J. B. Shukla

Editing of final manuscript: Arti Saxena, Vijay Kumar, J. B. Shukla

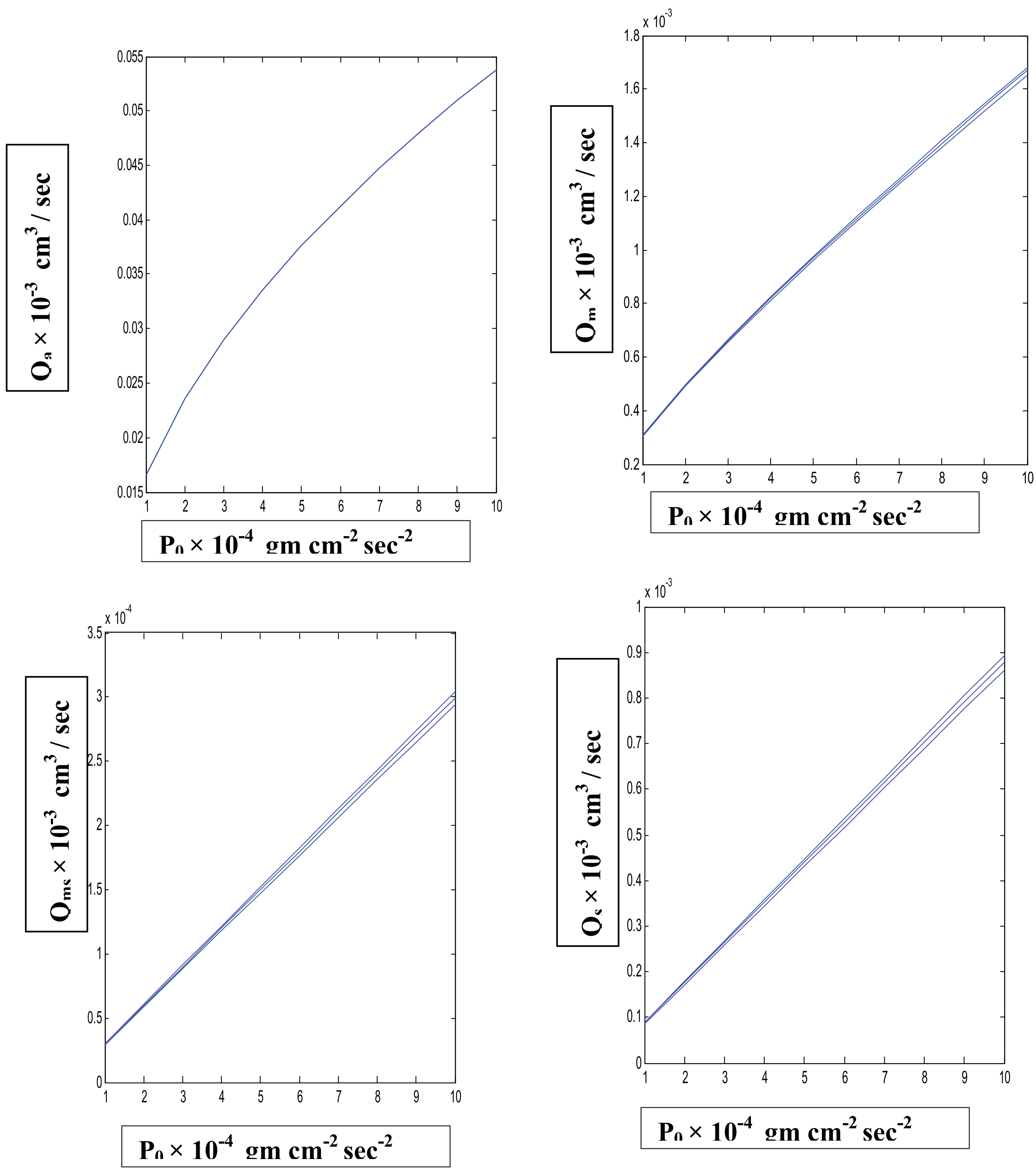

Figure 4.1: Variation of Q_a, Q_m, Q_{ms} and Q_s with P_0 for different μ_s

($\mu_{ms} = 0.5\,poise$, ϕ_s = 0.05 gm^{-1} cm^2 sec)

Upper denotes μ_s =0.01 poise

Middle denotes μ_s =0.05 poise

Lower denotes μ_s =0.1 poise

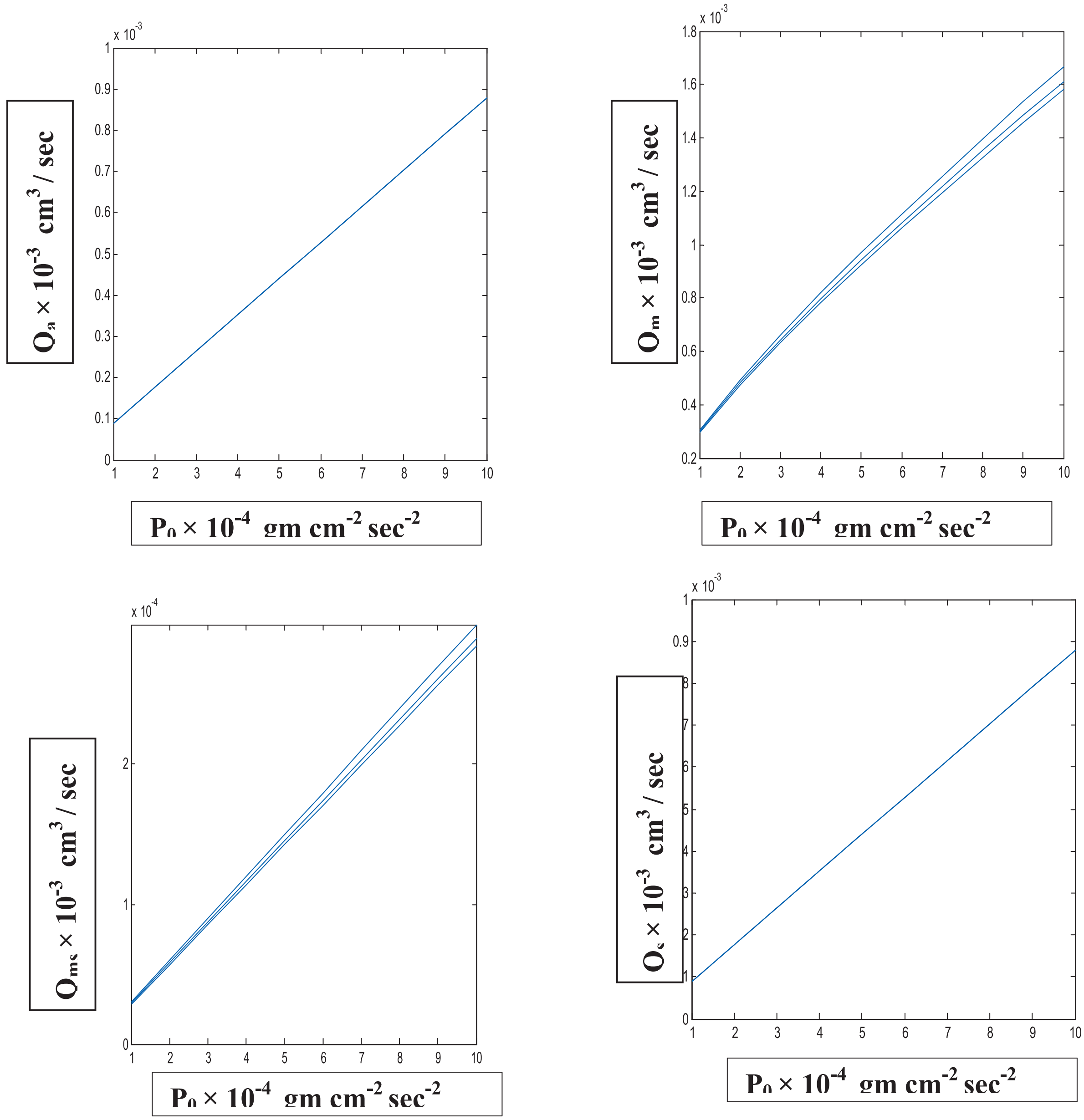

Figure 4.2: Variation of Q_a, Q_m, Q_{ms} and Q_s with P_0 for different μ_{ms}

(μ_s =0.05 poise, ϕ_s= 0.05 gm^{-1} cm^2 sec)

Upper denotes $\mu_{ms} = 0.5\, poise$

Middle denotes $\mu_{ms} = 0.7\, poise$

Lower denotes $\mu_{ms} = 0.9\, poise$

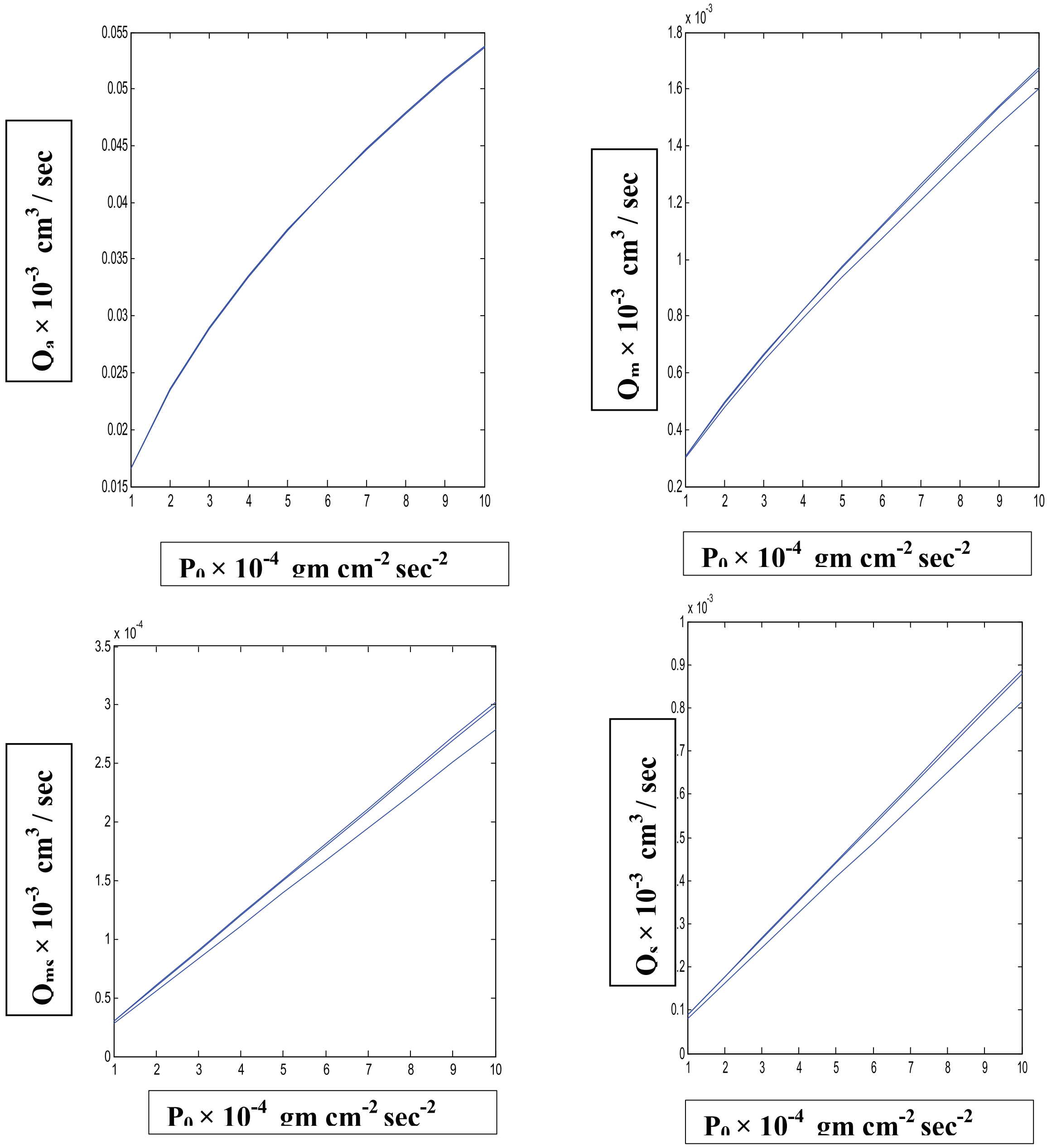

Figure 4.3: Variation of Q_a, Q_m, Q_{ms} and Q_s with P_0 for different ϕ_s

($\mu_{ms} = 0.5 poise$, $\mu_s = 0.05$ 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 =0.01 gm^{-1} cm^2 sec

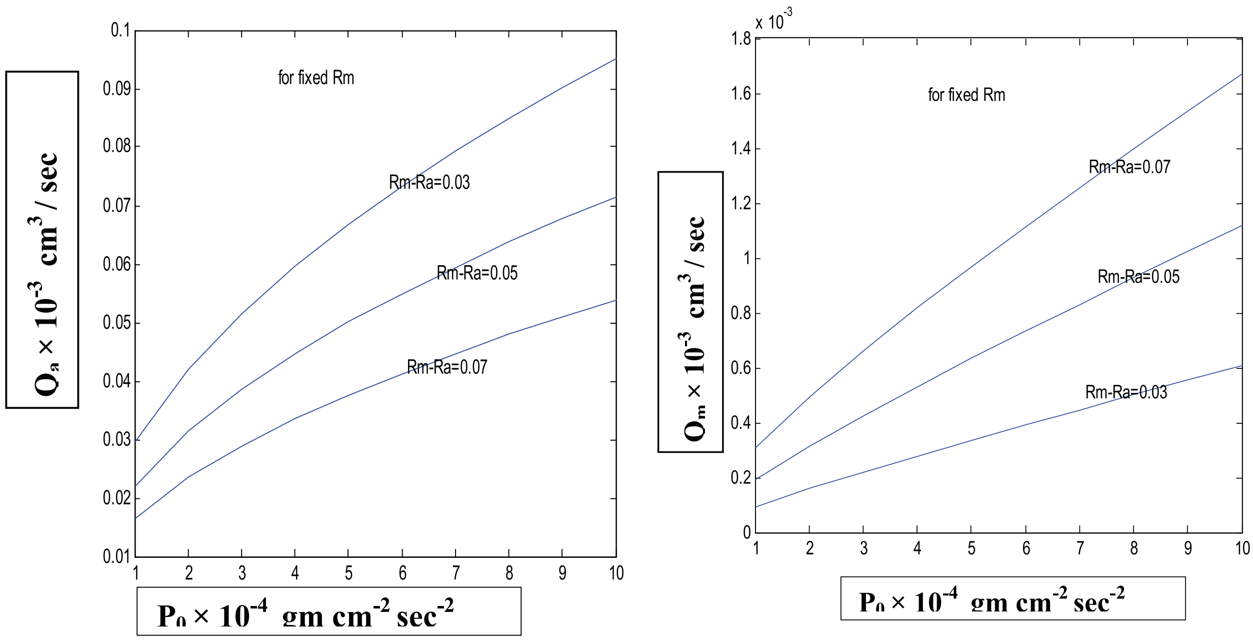

Figure 4.4a: Variation of Q_a and Q_m with P_0

($\mu_s = 0.05$ poise, $\mu_{ms} = 0.5\,poise, \phi_s$ =0.05 gm^{-1} cm^2 sec)

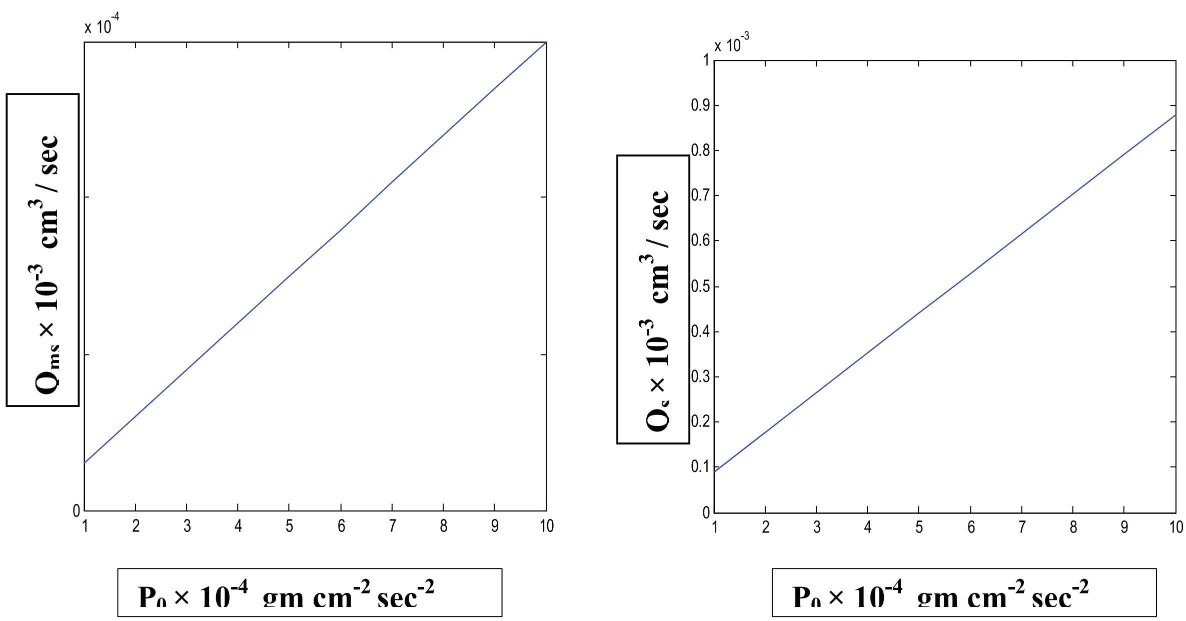

Figure 4.4b: Variation of Q_{ms} and Q_s with P_0

($\mu_s = 0.05$ poise, $\mu_{ms} = 0.5\,poise, \phi_s$ =0.05 gm^{-1} cm^2 sec)

Upper denotes $(R_m - R_a)$ =0.09 cm

Middle denotes $(R_m - R_a)$ =0.08 cm

Lower denotes $(R_m - R_a)$ =0.07 cm

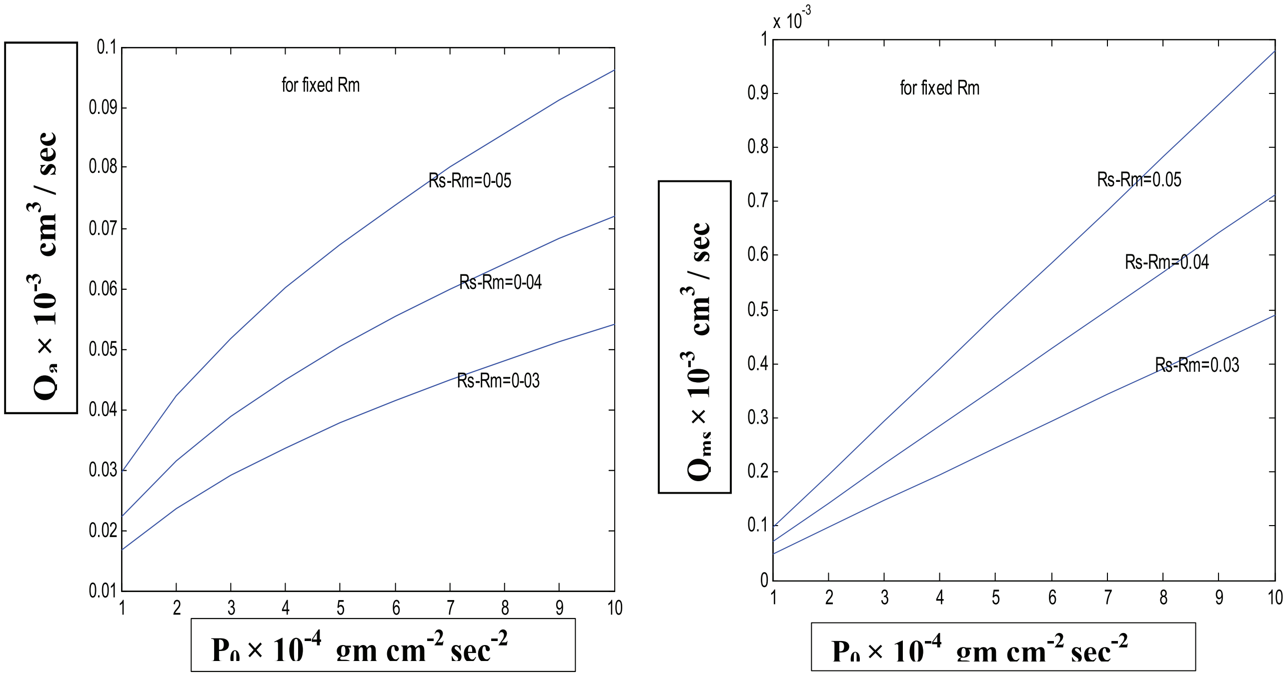

Figure 4.5a: Variation of Q_a, Q_{ms} with P_0

μ_s (= 0.05 poise, $\mu_{ms} = 0.5 poise$, ϕ_s =0.05gm^{-1}cm^2 sec)

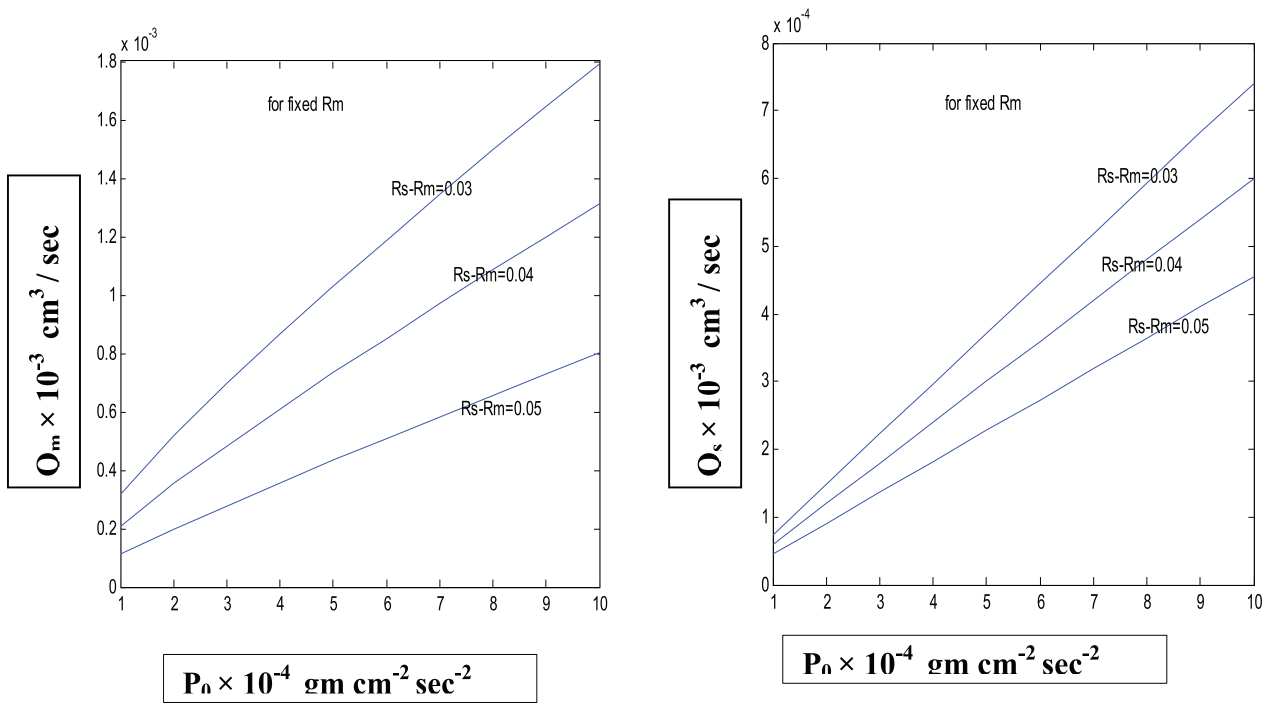

Figure 4.5b: Variation of Q_m, Q_s with P_0

(μ_s = 0.05 poise, $\mu_{ms} = 0.5 poise$, ϕ_s =0.05 gm^{-1} cm^2 sec)

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