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Mathematical model on two phase hepatic blood flow in capillary during malaria

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Abstract
The present work is aimed to study non-Newtonian power law model for two phase blood flow in hepatic capillary in case of malaria. According to Fahreaus-Lindqvist affect the blood flow in two separated layers when it enters into capillaries. The first layer is along the surface of the capillaries containing plasma and the second layer is core layer containing blood cells. In this study we applied Navier-Stoke's equation and equation of continuity for cylindrical co-ordinate system and all required equations presented in tensorial form. We calculated the value of parameter with the help of numerical method for clinical data and found a linear relationship between blood pressure drop and hematocrit. Finally, the graphical representation helps to verify of the proposed model.

Keywords: Hepatic circulation, malaria, hematocrit, viscosity, capillary, fahreaus-lindqvist effect

1. Introduction

1.1 Structure and Function of Liver: The liver is an important metabolic organ and has the most complicated circulation. Its dual blood supply is divided between the hepatic artery, which delivers 25%-30% of the blood supply and portal vein, which contributes about 70%-75% of blood supply to the liver and is rich in nutrients required for liver metabolism and while the hepatic artery can control and regulate the blood flow through the liver [30]. The arterial and portal blood ultimately mixes within the hepatic sinusoids before draining into the systemic circulation via the hepatic venous system [29]. According to the anatomical peculiarity of the double afferent blood supply of the liver, the blood entering the liver is partially deoxygenated venous blood supplied by the portal vein, which collects all the blood that leaves the spleen, stomach, small and large intestine, gallbladder and pancreas [24].

1.2 Structure and Function of Capillary: Capillaries are micro vessels and the smallest blood vessels in human body. They are composed of the tunica intima consisting of a thin wall of simple squamous endothelial cells [33]. Sinusoidal capillaries or discontinuous capillaries are special type of open-pore capillary, also known as sinusoid that have wider fenestrations that are 30-40 micrometres in diameter, with wider openings in the endothelium [34]. Capillaries connect the arterial system which includes the blood vessels that carry blood away from heart to venous system and venous system includes the blood vessels that carry blood back to jheart. The exchange of oxygen, nutrients and waste between blood and tissues also happens in capillaries.

1.3 Composition of Blood: Blood is composed of blood cells suspended in liquid called blood plasma which constitute 55% of blood fluid is mostly water [31] and 45% formed components such as RBCs, WBCs and platelets. Blood account for 7% of human body weight [6, 32]. The blood collects oxygen from lungs and delivers it to various cells throughout the body. Blood is a lifesaving liquid organ. Whole is a mixture of cellular elements, colloids and crystalloids. As different blood components have different relative density, sediment rate and size they can be separated when centrifugal force is applied [35].

1.4 Description of Disease: Human infections begin with the bite of mosquito vector and release of malaria sporozoites, with the sporozoite then travelling to the liver and invading hepatocyte [4].

After rapid multiplication of liver stage parasites, the muture hepatic schizont ruptures and releases red blood cells invading merozoites into the blood stream. In the case of *P. falciparum*, after merozoite invasion of a RBC rupture and release of 16-32 new merozoites ensues [5]. The complications of the disease arise during the blood stage, which is characterized by symptoms such as cerebral malaria, severe anemia, metabolic acidosis and respiratory distress [2]. During the blood stage the parasites release toxic factors that contribute to inflammation. In addition, iRBCs secrete small vesicles that contain human and parasite-derived molecules [3].

2. Real Model

2.1 Choice of Frame of Reference: In this model we have chooses orthogonal curvilinear generalized three-dimensional co-ordinate system denoted by E^3 called three dimensional Euclidean space of the moving blood. All quantities related to blood flow written in tensorial form which is comparatively more realistic. Let P be any point in space with co-ordinate x^i with respect to axes O X^i, O as origin where i = 1, 2, 3. At any time t, $v^k = v^k$ (x^i, t) be velocity of blood, p = p (x^i, t) thermodynamically pressure and ρ = ρ (x^i, t) density. Since blood vessels are cylindrical the governing equations have to transform into cylindrical co-ordinates system

3. Basic Bio-Fluid Equation for Two Phases

According to Sherman I.W. and Sherman V.G. blood is mixed fluid. There are two phases in the blood, one is plasma and other is blood cells. The blood cells are enclosed with a semi –permeable membrane whose density is greater than that of plasma. These blood cells are uniformly distributed in plasma.

3.1 Equation of continuity for two phase blood flow

According to Upadhyay V. the flow of blood is affected by the presence of blood cells and this effect is directly proportional to the volume covered by blood cells. Let the volume portion covered by blood cells in unit volume be X, then the volume portion covered by plasma will be 1-X, where X=$\frac{H}{100}$ and H is hematocrit the volume percentage of blood cells. If the mass ratio of blood cells to plasma is r then

$$r = \frac{X\rho_c}{(1-X)\rho_p} \tag{3.1}$$

Where ρ_c and ρ_p are densities of blood cells and blood plasma respectively. The both phase the blood cells and plasma move with common velocity. Campbell and Pitcher have presented a model for this condition. Equation of continuity for two phase according to principle of conservation of mass defined by Kapoor J.N. and Gupta R. C. as follows

$$\frac{\partial(X\rho_c)}{\partial t} + (X\rho_c v^i)_{,i} = 0 \tag{3.2}$$

and

$$\frac{\partial(1-X)\rho_p}{\partial t} + \left((1-X)\rho_p v^i\right)_{,i} = 0 \tag{3.3}$$

Where v common velocity of two phase blood cells and plasma, $(X\rho_c v^i)_{,i}$ is covariant derivative of $(X\rho_c v^i)$ with respect to x^i and $\left((1-X)\rho_p v^i\right)_{,i}$ is covariant derivative of $\left((1-X)\rho_p v^i\right)$ with respect tox^i.

If ρ_m be uniform density of blood then

$$\frac{1+r}{\rho_m} = \frac{r}{\rho_c} + \frac{1}{\rho_p} \text{ where } \rho_m = X\rho_c + (1-X)\rho_p \tag{3.4}$$

Combined equation (3.2) and (3.3) and using (3.4) we get

$$\frac{\partial\rho_m}{\partial t} + (\rho_m v^i)_{,i} = 0 \tag{3.5}$$

3.2 Equation of motion for two phase blood flow-

According to Ruch T.C. and H.D. the hydro dynamical pressure p between two phases of can be supposed to be uniform because the both phases are always in equilibrium state in blood. According to principle of conservation of momentum the equation of motion of two phase blood cells and plasma

$$X\rho_c \frac{\partial v^i}{\partial t} + (X\rho_c v^j)v^i_{,j} = -Xp_{,j}g^{ij} + X\eta_c\left(g^{jk}v^i_{,k}\right)_{,j} \tag{3.6}$$

And

$$(1\text{-}X)\rho_p \frac{\partial v^i}{\partial t} + \{(1-X)\rho_p v^j\}v^i_{,j} = -(1-X)\, p_{,j} g^{ij} + (1-X)\eta_p \left(g^{jk} v^i_{,k}\right)_{,j} \quad (3.7)$$

Now adding (3.6) and (3.7) and using (3.4) then equation of motion for blood flow will be

$$\rho_m \frac{\partial v^i}{\partial t} + (\rho_m v^j) v^i_{,j} = -p_{,j} g^{ij} + \eta_m \left(g^{jk} v^i_{,k}\right)_{,j} \quad (3.8)$$

Where, $\eta_m = X\eta_c + (1-X)\eta_p$ is the viscosity coefficient of blood as a mixture of two phases.

3.3 Mathematical Modeling

The constitutive equation for blood vessel is

$T' = \eta_m e^n + T_p$ Or, $T' - T_p = \eta_m e^n = T_e$ where T_e is effective stress whose generalized form will be $T^{ij} = -pg^{ij} + T_e^{ij}$

where $T_e^{ij} = \eta_m\, (e^{ij})^n$ and $e^{ij} = g^{jk} v^i_k$

Equation of continuity - $\frac{1}{\sqrt{g}} (\sqrt{g} v^i)_{,i} = 0$ (3.9)

Equation of motion - $\rho_m \frac{\partial v^i}{\partial t} + \rho_m v^j v^i_{,j} = -T^{ij}_{e,j}$ (3.10)

Where all the symbols have their usual meaning

Let x^1 = r, x^2 = θ and x^3 = z be cylindrical co-ordinates and square length of small element $ds^2 = dr^2 + r^2\, d\theta^2 + dz^2$

Christoffel's symbols of first and second kind are given below.

$[i\ j,\ k] = \frac{1}{2}\left[\frac{\partial g_{jk}}{\partial x^i} + \frac{\partial g_{ik}}{\partial x^j} - \frac{\partial g_{ij}}{\partial x^k}\right]$ and $\begin{Bmatrix} k \\ ij \end{Bmatrix} = g^{k\alpha}[ij, \alpha]$

$[g_{ij}]$ be matrix of metric tensor and $[g^{ij}]$ be matrix of conjugate matrix tensor where $[g_{ij}] = \begin{bmatrix} 1 & 0 & 0 \\ 0 & r^2 & 0 \\ 0 & 0 & 1 \end{bmatrix}$ $[g^{ij}] = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \frac{1}{r^2} & 0 \\ 0 & 0 & 1 \end{bmatrix}$

Metric elements g_{rr} = 1, $g_{\theta\theta} = r^2$, g_{zz} = 1

Or, g_{11} = 1, $g_{22} = r^2$, g_{33} = 1

Christoffel's symbols of second kind for cylindrical co-ordinates

$\begin{Bmatrix} 1 \\ 22 \end{Bmatrix} = -r, \begin{Bmatrix} 2 \\ 21 \end{Bmatrix} = \begin{Bmatrix} 2 \\ 12 \end{Bmatrix} = \begin{Bmatrix} 1 \\ r \end{Bmatrix}$ Except these all components are zero

Physical components

Since $\sqrt{g_{11}}\, v^1 = v_r$ or, $v_r = v^1$

$\sqrt{g_{22}}\, v^2 = v_\theta$ or, $v_\theta = rv^2$

and $\sqrt{g_{33}} v^3 = v_z\, or, v_z = v^3$

Matrix of physical components of shearing stress tensor

$$\tau'^{ij} = \eta_m\, (e^{ij})^n = \eta_m \left(g^{jk} v^i_{,k} + g^{ik} v^j_{,k}\right)^n \quad (3.11)$$

$$\tau'^{ij} = \begin{bmatrix} 0 & 0 & \eta_m \left(\frac{dv}{dr}\right)^n \\ 0 & 0 & 0 \\ \eta_m \left(\frac{dv}{dr}\right)^n & 0 & 0 \end{bmatrix}$$

The covariant derivative of τ'^{ij}

$$\tau'^{ij}_{,j} = \frac{1}{\sqrt{g}} \frac{\partial}{\partial x^j} (\sqrt{g} \rho^{ij} + \begin{Bmatrix} i \\ j\ k \end{Bmatrix} \quad (3.12)$$

4. Analysis and Solution

According the above facts, the governing tensorial equation can be transformed into cylindrical form which is as follow

The equation of continuity $\frac{\partial v}{\partial z} = 0$ (4.1)

The equation of motion

r – Component $-\frac{\partial p}{\partial r} = 0$ (4.2)

Θ - Component $0 = 0$ (4.3)

z- Component $-\frac{\partial p}{\partial z} + \frac{\eta_m}{r}\frac{\partial}{\partial r}\left[r\left(\frac{\partial v_z}{\partial r}\right)^n\right] = 0$ (4.4)

Here this fact has been taken in view that the blood flow is axially symmetric in arteries concerned i.e. $v_\theta = 0$ and v_r, v_z and p do not depend upon Θ and also blood flow radial.

$\frac{\partial p}{\partial t} = \frac{\partial v_r}{\partial t} = \frac{\partial v_\Theta}{\partial t} = \frac{\partial v_z}{\partial t} = 0$

From (4.1) $v_z = v(r)$ (4.5) since v does not depend upon θ

From equation (4.2) p = p (z) (4.6)

Because p does not depend upon Θ using equation (4.5) & (4.6) in (4.4) then

$-\frac{\partial p}{\partial z} + \frac{\eta_m}{r}\frac{d}{dr}\left[r\left(\frac{dv}{dr}\right)^n\right] = 0$ (4.7)

The pressure gradient $-\frac{dp}{dz}$ = P of blood flow in capillaries remote from liver can be supposed to be constant, therefore equation (4.7) takes the following form

$\frac{d}{dr}\left[r\left(\frac{dv}{dr}\right)^n\right] = -\frac{Pr}{\eta_m}$ (4.8)

On integrating (4.8) we obtain

$r\left(\frac{dv}{dr}\right)^n = -\frac{pr^2}{2\eta_m} + A$ (4.9)

Since the velocity of blood flow on the axis of the cylindrical capillary is maximum and constant so we apply the boundary condition at r=0, $v = v_0$ (constant) on equation (4.11) we get A=0 then equation (4.9) takes the following form.

$r\left(\frac{dv}{dr}\right)^n = -\frac{p\,r^2}{2\eta_m}$ or, $-\frac{dv}{dr} = \left(\frac{pr}{2\eta_m}\right)^{1/n}$

(4.10)

Again integrating (4.10) we get

$$v = -\left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} \frac{r^{\frac{1}{n}+1}}{\frac{1}{n}+1} + B$$

(4.11)

Now we apply no slip condition r= R(radius of blood vessel) and $v = 0$ in (4.11) then we obtain

$$B = \left(\frac{P}{\eta_m}\right)^{\frac{1}{n}} \frac{n}{n+1} R^{\frac{1}{n}+1}$$ (4.12)

From (4.11) and (4.12) we have

$$v = \left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} \frac{n}{n+1}\left[R^{\frac{1}{n}+1} - r^{\frac{1}{n}+1}\right]$$ (4.13)

This is velocity of blood flow in capillary.

5. Two layered blood flow in which one layer is Newtonian while other layer is non Newtonian

Now velocity of blood flow in Newtonian case is as follows:

$$v_p = \frac{P}{4\eta_p}(R^2 - r^2);\ R - \delta \le r \le R \tag{5.1}$$

Where δ is radius of core layer

The velocity of core layer is as follows:

$$v_m = \left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} \frac{n}{n+1}\left[R^{\frac{1}{n}+1} - r^{\frac{1}{n}+1}\right] + \left[\frac{P}{4\eta_p}\{R^2 - (R-\delta)^2\} - \left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} \frac{n}{n+1}\left\{R^{\frac{1}{n}+1} - (R-\delta)^{\frac{1}{n}+1}\right\}\right]; \tag{5.2}$$

$$0 \le r \le R - \delta$$

Where, the second term is the relative velocity of plasma layer with respect to core layer

5. Result

The flow flux of blood in capillaries is

$$Q = \int_0^{R-\delta} v_m\, 2\pi r dr + \int_{R-\delta}^{R} v_p\, 2\pi r dr$$

$$Q = \int_0^{R-\delta} \left[\left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} \frac{n}{n+1}\left(R^{1+\frac{1}{n}} - r^{\frac{1}{n}+1}\right) + \frac{P}{4\eta_p}\{R^2 - (R-\delta)^2\} - \left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} \frac{n}{n+1}\left\{R^{\frac{1}{n}+1} - (R-\delta)^{\frac{1}{n}+1}\right\}\right] 2\pi r dr + \int_{R-\delta}^{R} \frac{P}{4\eta_p}(R^2 - r^2)\, 2\pi r dr$$

$$Q = \pi \frac{n}{3n+1}\left(\frac{P}{2\eta_m}\right)^{\frac{1}{n}} (R-\delta)^{\frac{1}{n}+3} + \pi \frac{P}{8\eta_p}\left[R^4 - (R-\delta)^4\right] \tag{5.3}$$

6. Observations: Hemoglobin and blood pressure is taken from

District Hospital Banda
Patient Name – Suresh Prasad Age – 48 years / male, Annual No. - 0935/2022
Clinic- Dr. S D Tripathi, Physician District Hospital Banda

Table 1: Haemoglobin vs blood pressure drop

S. No	Date	B.P (In mm hg)	Hemoglobin (gm/dl)	Hematocrit (H)	B.P (In Pascal)	BPD
1	10/09/2022	135/90	11.1	33.3	17998.2/11998.8	-2999.7
2	12/09/2022	138/92	10.6	31.8	18398.16/12265.44	-3066.36
3	14/09/2022	132/86	9.8	29.4	17598.24/11465.52	-2888.6
4	17/09/2022	135/88	9.5	28.5	17998.2/11732.16	-2955.26
5	19/09/2022	130/82	9.7	29.1	17331.6/10932.24	-2784.91

Average systolic pressure= 17864.88 pa

Average diastolic pressure=11678.832 pa

Capillary pressure drops in Pascal second = $\frac{2}{3}\left[\frac{\frac{S+D}{2}+D}{3}\right] - \left[\frac{\frac{S+D}{2}+D}{3}\right]$

Average hematocrit H= 30.42

Q = 1000 ml/min = 0.01666 litre/sec = $1.67\times 10^{-5} m^3/sec$

According to Gustafaon and Daniel R, (1980)

η_p = 0.0015 (Pascal-Sec)

According to Glenn Elert (2010)
η_m = 0.035 (Pascal –Sec)

R= radius of capillary=35×10^{-6} meter

δ=thickness of RBC layer = $\frac{1}{3}$R=$\frac{1}{3}$ 35×10^{-6}=11.66×10^{-6}meter

R-**δ**= (35-11.67) $\times10^{-6}$=23.33×10^{-6}meter

Average length of hepatic capillary= 615µm=615×10^{-6} meter

H=average hemaocrit= 30.42, Blood pressure drop = 2938.97 (Pascal)

Since η_m = η_c x + η_p (1-X) where X= $\frac{H}{100}$

Substituting the values of η_m, η_p, and H in above relation we get η_c = 0.1116249 again from above relation

η_m = 110.1249H + 0.0015

Since P = - $\frac{dp}{dz}$ or, dp = -Pdz

Where $p_f - p_i$ pressure drop and $z_f - z_i$ = length of hepatic capillary

Substituting the values of Q, $(p_f - p_i)$, $(z_i - z_f)$ and η_m in above equation

We obtain, 418784493= $(1592.71)^{\frac{1}{n}}$ $\frac{n}{3n+1}$

Or, n log $\frac{n}{3n+1} - 8.62199059\ n + 3.20213671 = 0$

Or, f $(x) =$ x log $\frac{x}{3x+1} - 8.62199059\ x + 3.20213671 = 0$

And d f $(x) =$ log $\frac{x}{3x+1} + \frac{1}{3x+1} - 8.62199059$

Solve above equation by Newton- Raphson method

$$x_{n+1} = x_n - \frac{f(x_n)}{f'(x_n)}$$

X*log(x/((3*x)+1))-(8.62199059*x)+ 3.20213671=0

Programme:

%% Ingredients

F=@(x) x*log(x/((3*x)+1))-(8.62199059*x)+ 3.20213671

DF=@(x) log(x/((3*x)+1))+1/((3*x)+1)- 8.62199059;

E=10^-4;

X0=0.5;

N=10;

% processing

If DF(x0)~=0

For i=1:N

X1=x0-f(x0)/DF(x0);
FPRINTF ('x%d =%.4f\n', i,x1)

If abs(x1-x0) & lt; e

Break end

If DF(x0)=0

Disp ('Newton raphson failed')
End

X0=x1;

End
Else

Disp ('Newton Rapson failed');
End

Answer:

& GT; & GT; NR_method

X1 = 0.3445

X2 = 0.3412

X3 = 0.3502

X4 =0.3408

X5 = 0.3408

Or, n = 0.3408

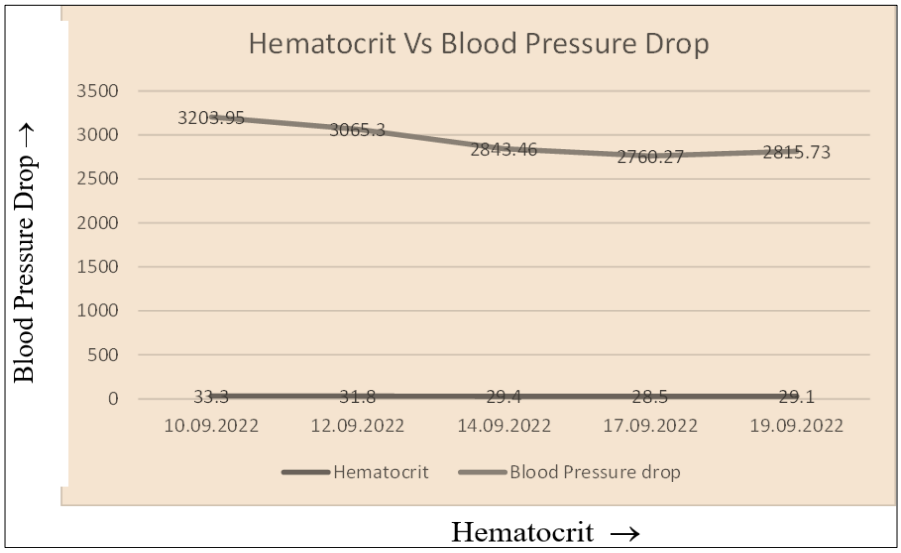
Substituting the value of η_m, Q and n we get

$p_f - p_i$ = 92.43398 H + 125.903379 (5.3)

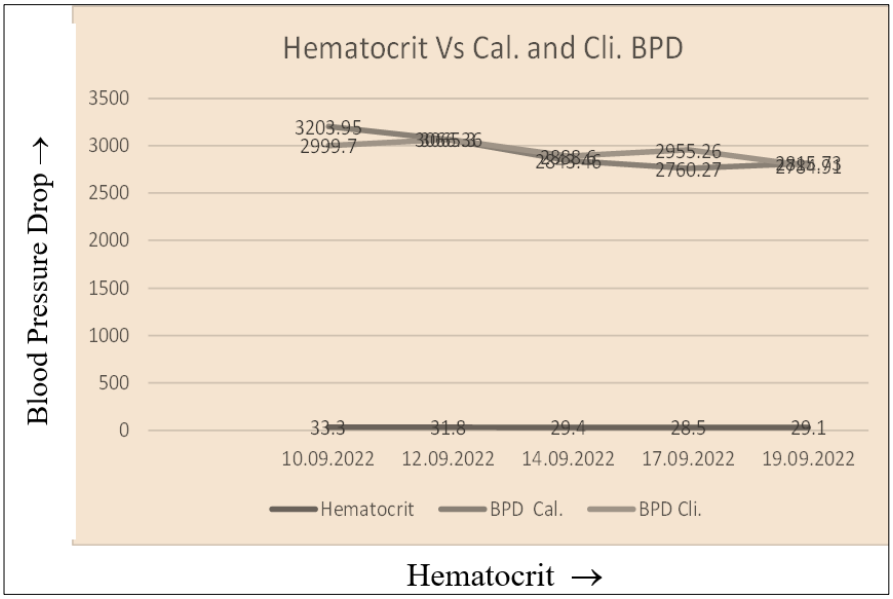
This is linear relationship between hematocrit and blood pressure drop

Table 2: Hematocrit vs mathematically modulated blood pressure drop

Date	10/09/2022	12/09/2022	14/09/2022	17/09/2022	19/09/2022
Hematocrit (H)	33.3	31.8	29.4	28.5	29.1
Blood pressure drop (ΔP)	3203.95	3065.30	2843.46	2760.27	2815.73



Graph 1: Hematocrit v/s modulated blood pressure drop



Graph 2: Hematocrit V/s (Modulated and Clinically) Blood Pressure Drop

7. Observation of graph

The graph-1 between blood pressure drop and hematocrit shows that five different dates were observed minimum blood pressure drop 2760.27 on dated 17/09/2022 and maximum value obtains 3203.95 on dated10/09/2022. At the hematocrit value from 33.3 to 28.5 via 31.8 and 29.4 the blood pressure drop straightly decreases on dated from 10/09/2022 to 17/09/2022 via 12/09/2022 and 14/09/2022 and hematocrit value from 28.5 to 29.1 the blood pressure drop straightly increases on dated from 17/09/2022 to 19/09/2022. The graph-2 shows that the comparative study of two graph (i) Graph hematocrit Vs clinical blood pressure drop (ii) Graph hematocrit Vs mathematically modulated blood pressure drop.

8. Conclusion

In graph-1 slope of straight line is absolute value and when hematocrit increases the blood pressure drop also increases and when hematocrit decreases the blood pressure drop also decreases. When trend of straight line decreasing sense then medicine dose slowly increases, when steepness of curve low then we can give high dose of medicine and when trend of straight line increasing sense then we suggest normal dose of medicine. Comparative studies of graphs show that both graphs have nearly same character and power law model verified for clinical data of malaria patient.

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