International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Deciphering Sickle Cell Dynamics: A Mathematical Modeling and Comparative Analysis Approach

Ashik Babu Parambath

Advanced Instrumentation Research Facility, Jawaharlal Nehru University, New Delhi-110067, India
Email: *ashikbabup987[at]gmail.com*

Abstract: ***Sickle cell disease (SCD) arises from a genetic mutation that changes a specific protein in red blood cells. This study explores the intricacies of SCD through the use of mathematical modeling and comparative analysis. By combining concepts from mathematics, biology, and computational science, we aim to decode the mechanisms driving this disease. Our mathematical framework assesses fluid flow dynamics in the context of SCD, taking into account the altered geometry of deformed red blood cells near the arterial walls. In our model, we simulate blood flow in a cylindrical, capillary-like duct to represent the passage of a single sickle cell interacting with the endothelial wall and the surrounding plasma. This approach allows us to observe how these deformed cells affect the flow of blood under various conditions, including the polymerization of hemoglobin and the dynamics of oxygen transport. The results reveal that as the axial velocity increases, so does the pressure within the vessel. We also found that regions of low viscosity are associated with lower pressure and velocity, while areas with higher viscosity exhibit increased pressure and velocity. Moreover, our comparative analysis of mathematical models and experimental data provides deeper insights into the pathophysiology of SCD and potential therapeutic approaches. This study not only enhances our understanding of the fluid dynamics involved in SCD but also suggests avenues for improved treatment strategies.***

Keywords: Fluid flow, sickle cell disease, mathematical modeling, comparative analysis, viscosity, pressure, velocity, endothelial wall, red blood cells, capillary, porous tube wall.

1. Introduction

Sickle cell disease, an inherited condition, arises from a recessive gene mutation that distorts red blood cells, leading to profound anemia in individuals with two copies of the mutated gene (homozygous) and milder symptoms in those carrying only one copy (heterozygous carriers). It is characterized by abnormal hemoglobin molecules, resulting in the deformation of red blood cells (RBCs) into a sickle shape [8,15,36, 43]. Despite decades of research, SCD remains a significant global health burden, particularly in regions where it is prevalent. Sickle Cell Disease is primarily considered a hereditary form of anemia resulting from a single mutation at the 6th codon of the β-globin chain of adult hemoglobin [6,17,23,42]. This mutation leads to the formation of hemoglobin tetramers that are more prone to polymerization in low oxygen conditions. This polymerization process disrupts the normal morphology of the cells, reduces RBC deformability and alters membrane adhesive properties [11,21,38,53]. These abnormal adhesion and decreased deformability of RBCs are primary culprits behind blood vessel occlusion, known as vaso-occlusion, in SCD [13,26,39,51]. Vaso-occlusion represents the hallmark of the disease and is associated with severe pain, crises, widespread organ damage, and premature mortality. SCD is a severe and widespread monogenic disorder, affecting millions worldwide and over 100,000 individuals in the United States alone [5,14,25,86]. The manifestations of SCD include chronic and acute crises, such as frequent pain episodes, silent cerebral infarction, early mortality, and organ damage []. Previous studies have highlighted the significant burden of Major Thalassemia in India, with thousands of affected children born each year. Current treatments for SCD focus on managing complications and symptoms, including blood transfusions, prophylactic penicillin, pneumococcal vaccination, and hydroxyurea therapy [7,27,31,45]. However, challenges remain, as blood transfusions may lead to iron overload without proper chelation therapy, and hydroxyurea treatment's efficacy varies among patients, raising concerns about long-term safety and uniform response. Understanding the complex dynamics of SCD is essential for improving patient outcomes and developing effective treatment strategies [4,16,48,89]. In this research paper, we embark on a scientific journey to explore the intricate mechanisms underlying SCD using mathematical modeling and comparative analysis. By integrating mathematical principles with biological insights, we aim to shed light on the pathophysiology of SCD and identify potential avenues for therapeutic intervention [3,29,33,69,88]. It circulates in a one-way direction from the heart, flowing through a network of vessels that progressively decrease in diameter from arteries to arterioles and capillaries, before returning to the heart via venules and veins, which gradually increase in diameter. In a healthy state, RBCs, which are biconcave discoid cells with a diameter of approximately 8 micrometers and a thickness of about 2 micrometers, account for 40-45% of the total blood volume [9,24,35,54,71,87]. RBCs are highly flexible cells capable of deforming to navigate through capillaries with internal diameters smaller than their own, facilitating the transport of oxygen and nutrients to various tissues throughout the body via the vascular network. Upon deoxygenation within microcirculation, hemoglobin molecules undergo a configuration change, leading to polymerization and the formation of rigid HbS fibers. These fibers distort and damage membrane and cytoskeleton of red blood cells (RBCs), resulting in new biomechanical and rheological properties [2,19,32,47,61,90].

Vaso occlusion, key event in SCD morbidity and mortality, manifests as painful condition. Sickle cell patients exhibit higher blood viscosity even under oxygenated conditions, attributed to reduced RBC deformability and plasma viscosity, which increases concentration of protein and promotes RBC aggregation contributing to blood flow obstruction and vaso-occlusion. Abnormal blood rheology can be influenced by many factors [1,12,28,64,82]. Various techniques, including viscometry, filtration, ektacytometry, micropipette aspiration, and optical tweezers, have been utilized to study RBC deformability, mechanical properties, and adherence to endothelial cells. Studies using microfluidics and computational modeling have provided insights into the flow dynamics and deformation of RBCs in microvessels [18,40,52,73,79]. A mathematical approach to predicting rheological properties, based on known mechanical properties of individual blood cells, is good for modeling blood flow in capillaries with diameters less than about 8 micrometers [10,34,49,60,72,81]. Numerous investigations in microcirculation have extended different models to study effects of plasmatic layer. Some assumed the undeformed shape of RBCs near wall to be parabolic, with deformation proportional to local pressure [20,44,57,67,76]. Others, assumed axisymmetric geometry of RBCs in analyzing capillary flow at low velocities. It was also represented that the cell as a bullet-like shape with isotropic tension on the wall. Numerical simulations by previous researchers investigated axisymmetric, pressure-driven RBC motion in cylindrical tube capillaries, exploring many parameters [22,56,63,68,80]. It was also studied that the effect of undeformed cell diameter on capillary flow [30,58,74,84]. Some of them have discussed the concentration profile of dissolved nutrients and penetration depth in tissues under diseased conditions [37,62,75]. Our study focus is on flow dynamics within capillaries, particularly concerning cell deformation. Consequently, we formulated a boundary value problem that couples the deformation and motion of the cell to the blood flow dynamics in the microcirculation [41,50,78]. In addition to mathematical modeling, we conduct a comparative analysis to validate our findings against experimental data and existing literature. This involves comparing the predictions of our mathematical models with empirical observations from clinical studies, in vitro experiments, and animal models of SCD.

2. Mathematical Formulation of the problem

Central to our investigation is the development and application of mathematical models to simulate the behavior of sickle cells within the bloodstream. These models are based on principles of fluid dynamics, polymer physics, and cell biomechanics, allowing us to capture the complex interactions between RBCs, hemoglobin molecules, and the surrounding microenvironment. By incorporating parameters such as hemoglobin concentration, oxygen saturation levels, and shear stress, we simulate the dynamic processes of hemoglobin polymerization, RBC sickling, and vaso-occlusive events [46,59,70]. Our mathematical models provide valuable insights into the spatiotemporal evolution of SCD-related phenomena, offering a quantitative framework for understanding disease progression. A set of mathematical expression has been developed for the 2D Cartesian geometry within the capillary. Red cell is approximately equal in size of the capillary diameter. In this model, red cell is represented by having an incompressible fluid internally and deforms axisymmetrically. The flow is assumed to occur in a single-file manner, and interactions between cells are neglected for simplicity. The governing equations for the motion is as below:

$$\frac{Du'}{Dt} = -\frac{1}{\rho}\nabla P' + \frac{\mu}{\rho}\nabla^2 u' \qquad (1)$$

Continuity equation, we have,

$$\frac{\partial u'}{\partial x'} + \frac{\partial v'}{\partial y'} = 0 \qquad (2)$$

Hence equation for motion is as below:

$$\frac{\partial P'}{\partial y'} = 0 \qquad (3)$$

$$-\frac{\partial P'}{\partial x'} + \mu\frac{\partial^2 u'}{\partial y'^2} = 0 \qquad (4)$$

$$h' = (\alpha+\beta)(P' - P'_0) + \frac{x'^2}{4a} \qquad (5)$$

where, P' = Pressure in fluid film, P'_0 = Pressure, a = Length, α and β = Radial compliances of tube and the cell, $(\alpha+\beta)'(P' - P_0)$ = Deformation parameter, U_0 and V_0 =Velocity of cell and plasma.

Non- Dimensional Scheme:

$x = x'/l,\ y = y'/H,\ P = P'/\rho V_0^2,\ u = u'/V_0,$
$P_0 = P'/\rho V_0^2,\ v = v/V_0,\ Re = \rho V_0 H/\mu,\ \sigma = \sigma'/(H)$ (6)

where, H = Radius of capillary, Re = Reynolds's number.

Boundary and matching condition:

$$\left.\begin{aligned} u' &= U_0 \quad && at \quad y' = h' \\ u' &= -\sigma'\frac{\partial u'}{\partial y'} \quad && at \quad y' = 0 \end{aligned}\right\} \qquad (7)$$

$$\left.\begin{aligned} v' &= 0 \quad && at \quad y' = h' \\ v' &= -\frac{K}{\mu}\frac{\partial \overline{P'}}{\partial y'} \quad && at \quad y' = 0 \end{aligned}\right\} \qquad (8)$$

Governing equation in dimensionless form: (Considering the effect of Renold's number in the system and using the above non-dimensional scheme, equation (3)-(5) are transformed as given below:

$$\frac{\partial P}{\partial y} = 0 \qquad (9)$$

$$\frac{\partial P}{\partial x} = \mathrm{Re}\frac{\partial^2 u}{\partial y^2} \qquad (10)$$

Thickness of fluid film is as below:

$$h = \alpha'\left(\frac{P}{P_0} - 1\right) + \xi x^2 \qquad (11)$$

Deformation parameter= $\xi = \frac{l^2}{4aH}$,

Radial complaiances of cell= $\alpha' = \frac{(\alpha+\beta)'\rho V_0^{\,2} P_0}{H}$

Boundary and matching condition in Dimensionless form:

$$\left.\begin{aligned} u &= \frac{U_0}{V_0} && at \quad y = h \\ u &= -\sigma\frac{\partial u}{\partial y} && at \quad y = 0 \\ v &= 0 && at \quad y = h \end{aligned}\right\} \quad (12)$$

Solution of the problem: This statement suggests that the equation governing the motion of the system has been solved, taking into account the provided boundary conditions. As a result of solving this equation, the solution for the axial velocity has been obtained. In other words, the velocity along the axis of the flow has been determined based on the specified conditions and the governing equation.

$$u = \mathrm{Re}\frac{dP}{dx}\left[y^2 - h^2\left[\frac{y-\sigma}{h-\sigma}\right]\right] + \frac{U_0}{V_0}\left[\frac{y-\sigma}{h-\sigma}\right] \quad (13)$$

3. Results and Discussion

In sickle cell anemia, prolonged lack of oxygen causes red blood cells (RBCs) to take on a sickled shape. Similarly, when normal RBCs are deformed for an extended period using micropipette aspiration, they also become permanently stabilized in an abnormal shape. By merging math with biology, we deepen our understanding of SCD's complexities and potential treatments. Our work adds to SCD knowledge and provides a quantitative way to analyze the disease. Looking ahead, interdisciplinary collaboration is crucial for tackling SCD challenges globally [55,83]. Moreover, our findings offer insights for developing new SCD therapies. By identifying disease mechanisms, we pinpoint targets for drugs and gene therapies. Our mathematical models also streamline therapy testing, speeding up drug development and cutting down on expensive clinical trials. Ultimately, our study opens doors to innovative SCD management strategies. The flow of red cell which taking the place in the exterior region of the RBC in the capillary the effect of reynolds number has been taken into account.

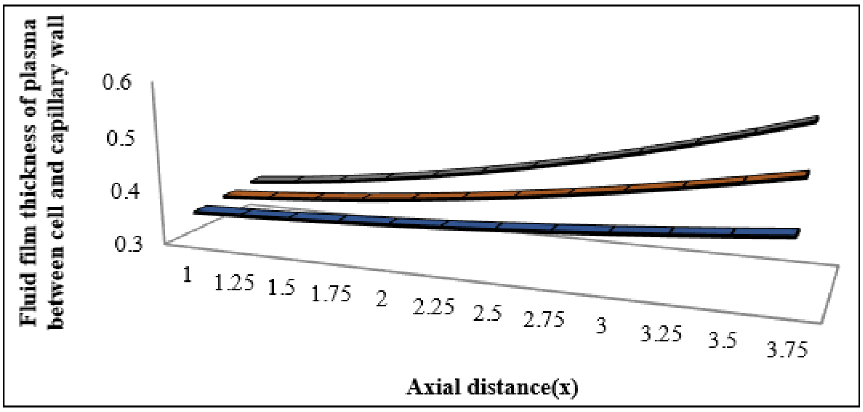

Figure 1: Plasma film thickness for axial distance (different deformation parameter)

In Figure (1), the results illustrated how the plasma film thickness (h) changes along the axial distance within the capillary for different values of the deformation parameter (e). This analysis provided insights into how the thickness of the plasma film surrounding the red blood cells varies as they travel through the capillary, considering different levels of deformation. The findings shown that film thickness of plasma between cell and capillary wall increases with an increase in the plasma film thickness [65,77]. Additionally, it is observed that the fluid film thickness of plasma between the cell and the capillary wall also increases with an increase in the deformation parameter. These results underscore the importance of mechanical interactions between blood cells and plasma in influencing the dynamics of blood flow within the microcirculation. Understanding these interactions is crucial for comprehending the complex behavior of blood as it navigates through narrow capillaries and vessels.

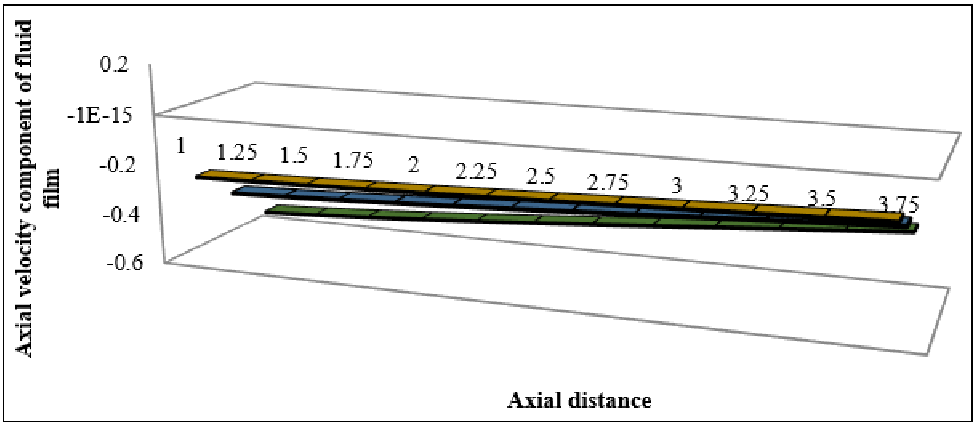

Figure 2: Axial velocity component for axial distance (different slip parameter)

Paper ID: SR24623002922 DOI: https://dx.doi.org/10.21275/SR24623002922

In Figure (2), the graph depicted how velocity component changes with axial distance along the capillary for various slip parameters. This visualization showcased variation in axial velocity component along length of the capillary for different slip parameters. It offers a clear understanding of how alterations in the slip parameter influence the velocity profile within the capillary [66,85]. Upon analyzing the graph, it is evident that the axial velocity increases with a decrease in the slip parameter. This observation highlighted the impact of slip conditions on the fluid velocity as it traverses through the capillary. Additionally, the graph indicated that axial velocity generally raises with an raise in the axial distance along the capillary.

4. Conclusion

This work presented a comprehensive investigation into the intricacies of SCD using mathematical modeling and comparative analysis. By integrating mathematical principles with biological insights, we gain deeper insights into the pathophysiology of SCD and identify potential therapeutic targets. Our findings contribute to the growing body of knowledge on SCD and provide a quantitative framework for understanding disease dynamics. The findings presented in this study provided valuable insights into the dynamics of blood flow within capillaries, particularly in the context of mechanical interactions between blood cells and plasma. The analysis revealed how the thickness of the plasma film surrounding red blood cells varies with both the plasma film thickness and the deformation parameter. These results underscore the significance of understanding mechanical interactions in influencing blood flow dynamics within microcirculatory systems. Furthermore, the visualization of axial velocity changes along the capillary for different slip parameters highlights the impact of slip conditions on fluid velocity.

References

[1] Akbar, S., Shah, S. R., "DURYSTA" the first biodegradable sustained release implant for the treatment of open-angle glaucoma, Int.J. of Frontiers in Bio. and Pharm Res., 01(02),1-7, 2021.

[2] Akbar, S., Shah, S. R., "Mathematical Modeling of Blood Flow Dynamics in the Cardiovascular System: Assumptions, Considerations, and Simulation Results", J. of Current Med. Res. & Opinion, 7(4), 2216-2225, (2024).

[3] Akbar, S., Shah, S. R., "The Effects of Prostaglandin Analogs on Intraocular Pressure (IOP) in Human Eye for Open Angle Glaucoma. Int. J. of Innovative Tech. and Exploring Eng.,10(2), 176-180, (2020).

[4] Anamika, Shah, S. R., "Mathematical and Computational study of blood flow through diseased artery", Int. J. of Computer Science, 5, (6), 1-6, (2017).

[5] Anamika, Shah, S. R., Anuradha "Bio-Computational analysis of blood flow through two phase artery", Int. J. of Engineering Science and Computing, 7, (6),13397-213401, (2017).

[6] Anamika, Shah, S. R., Kumar, R., "Mathematical Modelling of blood flow through tapered stenosed artery with the suspension of nanoparticles using Jeffrey fluid model", Int. J of development Res., 07, 06,13494-13500, (2017).

[7] Anamika, Shah, S. R., Singh A., "Mathematical Modelling Of Blood Flow through Three Layered Stenosed Artery", Int. J. for Res. in Appl. Sci. and Eng. Tech., 5, (6), 1-6, (2017).

[8] Anuradha S,, Shah, S. R., Siddiqui, S. U., "Effects of inclined multi-stenoses arteries on blood flow characteristics using bingham plastic fluid", Int. J. for Mathematics, 1, (12),7-14, (2015).

[9] Anuradha S., Shah, S. R., S.U. Siddiqui, "Mathematical Modeling and Numerical Simulation of Blood Flow through Tapered Artery", International Journal of Innovative Science, Engineering & Technology, 3, (2), 710-717, (2016).

[10] Anuradha S., Shah, S. R., S.U. Siddiqui, "Performance of blood flow through two phase stenosed artery using Herschel-Bulkley model", Int. Journal of Applied & Pure Science and Agriculture, 2, (2), 228-240, (2016).

[11] Anuradha S., Shah, S. R., Siddiqui, S. U., "Mathematical Modelling and Analysis of Blood Flow through Diseased Blood Vessels", International Journal of Engineering and Management Research, 5, (6), 366-372, (2015).

[12] Anuradha, S., Shah, S. R., Siddiqui, S. U., "A Mathematical Model to study the similarities of blood fluid models through inclined multi-stenosed artery", Int. J. of Eng. Research and Modern Edu., 2, (1), 108-115, (2017).

[13] Chaturvedi, P. and Shah, S. R. "Role of crizanlizumab for sicke red cells disease", International Journal of Biology, Pharmacy and Allied Sciences, 12(3), 1147-1157, (2023).

[14] Chaturvedi, P., Kumar, R., Shah, S. R., "Bio-Mechanical and Bio-Rheological Aspects of Sickle Red Cells in Microcirculation: A Math. Mod. Approach, Fluids, 2021, 6, 322, 01-15.

[15] Chaturvedi, P., Shah, S. R., "Mathematical Analysis for the Flow of Sickle Red Blood Cells in Microvessels for Bio Medical Application, Yale J. of Bio. and Medicine, 96 (1), (2023),13-21.

[16] Chaturvedi, P., Shah, S. R., Akbar, S., Kumar, R., "Prospective of Hydroxychloroquine and Zinc with Azithromycin for Nanoparticles Blood Flow in Covid-19 Patients, Int. J. of Nanotech. in Medicine & Eng. 6(1),01-07, (2021).

[17] Geeta, Siddiqui, S. U., Sapna, "Mathematical Modelling of blood flow through catheterized artery under the influence of body acceleration with slip velocity", Application and applied Math. An Int. J., 8(2), 481-494, (2013).

[18] Geeta, Siddiqui, S. U., Shah, S. R., "A Biomechanical approach to the effect of body acceleration through stenotic artery", Applied Math. and Computation, 109(1), 27-41, (2015).

[19] Geeta, Siddiqui, S. U., Shah, S. R., "Effect of body acceleration and slip velocity on the pulsatile flow of casson fluid through stenosed artery"Adv. Appl.Sci.Res.5(3),231-225, (2014).

[20] Geeta, Siddiqui, S. U., Shah, S. R.,"A Mathematical Model for two layered pulsatile blood flow through

stenosed arteries", E-Journal of Sci. and Technology, 109 (11), 27-41, (2015).

[21] Gupta, P., Akbar, S., Shah, S. R., Alshehri, Mo., Sharma, S. K., and "A Mathematical Study for Promoting Disability Inclusion in Glaucoma:A Comprehensive Approach", J. of Disability Res. 3,1-12, (2024).

[22] Islam S. M. N., Sadique, Mo., Shah, S. R., Sharma,S. K., "Effect of Significant Parameters on Squeeze Film Characteristics in Pathological Synovial Joints", Math.,11(1468)1-23, (2023).

[23] Jaiswal., K. M., Shabab Akbar and Shah S. R., Mo. Sadique "Exploring capillary-tissue fluid exchange: Insights into red cell deformation in narrow vessels and its clinical implications", International Journal of Fauna and Biological Studies, 11(3), 4-14, (2024).

[24] Kasturia, P., Rohit Kumar Sharma, Purnima Chaturvedi, Ravins Dohre, Shah, S. R.,"Efficacy of venetoclax and azacitidine for targeting leukemic stem cell in acute myeloid leukemia", International Journal of Biology, Pharmacy and Allied Sciences, 13(6), 3072-3090, (2024).

[25] Kaur, H., Prithvi Singh, Rubi Solanki, Alvea Tasneem, Simran Suri, Shah, S. R., Ravins Dohare, "Screening of miRNAs as prognostic biomarkers and their associated hub targets across Hepatocellular carcinoma using survival-based bioinformatics approach", Journal of Genetic Engineering and Biotechnology, 22 (1), 1-10, (2024).

[26] Kumar V., and Shah, S. R., "Mathematical model to study the heat transfer between core and skin", SRMS, Journal of Mathematical Sciences, 7,7-12, (2024).

[27] Kumar, J. P., Sadique, Mo. Shah, S. R.,, "Mathematical study of blood flow through blood vessels under diseased condition, Int. J. of Multidisciplinary Res. & Dev., 9(6), (2022), 31-44.

[28] Kumar, P, Shah, S. R., "A Hydromechanical Perspective to Study the Effect of Body Acceleration through Stenosed Artery", Int. J. of mathematical engineering and management sciences, 6 (5),1381-1390, (2021).

[29] Kumar, R., Shah, S. R., "A mathematical approach to study the blood flow through tapered stenosed artery with the suspension of nanoparticles" Destech Transactions on Engineering and Tech. Research,01,1-6, (2017).

[30] Kumar, R., Shah, S. R., "Mathematical Modeling of Blood Flow with the Suspension of Nanoparticles Through a Tapered Artery With a Blood Clot", Frontiers in Nanotech., 2, 596475, 1-5, (2020).

[31] Kumar, R., Shah, S. R., "Performance of blood flow with suspension of nanoparticles though tapered stenosed artery for jeffrey fluid model" Int. J. Nanosci.,17(6),1850004 (1-7), (2018).

[32] Kumar, R., Shah, S. R., "Study of blood flow with suspension of nanoparticles through tapered stenosed artery", Global J. of Pure and Applied Mathematics, 13(10), 7387-7399, (2017).

[33] Kumar, V., and Shah, S. R., "Mathematical modelling to study the heat transfer between core and skin", SRMS, Journal of Mathematical Sciences, 7 (2021), 7-12, (2024).

[34] Kumar, V., Shah, S. R., "A mathematical approach to investigate the temperature distribution on skin surface with sinusoidal heat flux condition, Int. J. of Multidisciplinary Research and Development, 9 (5), (2022), 141-146.

[35] Kumar, V., Shah, S. R., "A Mathematical study for heat transfer phenomenological processes in human skin", Int. J. of Mechanical Eng., 7 (6), (2022),683-692.

[36] Kumar, V., Shah, S. R., "Thermobiological Mathematical Model for the study of temperature response after cooling effects", ssrg, Int. J. of Applied physics, 9 (2), (2022), 7-11.

[37] Lenin, J. S., Shah S. R., "Mathematical Analysis of Stem Cell Dynamics in Acute Myeloid Leukemia: Towards Precision Medicine Strategies, Int. J. of Sci.&Res.13(05),528-535, (2024).

[38] Mahesh, Arya, S., Shah, S. R., "Optimizing cardiovascular health: ayurvedic insights into blood flow through normal and stenosed arteries, Int. Journal of AYUSH, 13 (5), 18-35, (2024).

[39] Majhi, L., Sudheer Arya Sapna Ratan Shah, "Exploring Shilajatu's Therapeutic Potential in Diabetes Management: A Comprehensive Study Integrating Ayurvedic Wisdom and Modern Science", International Journal of Science and Research (IJSR), 13(5), 1374-1380, (2024).

[40] Malik, M., Z., Kumar, R., Shah, S. R.,, "Effects of (Un)lockdown on COVID-19 transmission: A mathematical study of different phases in India, medRxiv The preprint server health Sci.,1-13, (2020).

[41] Mo. Sadique and Shah, S. R., "Mathematical model to study the study the squeeze film characteristics of synovial joints in diseased human knee joint", World Scientific Annual Review of Biomechanics, 1 (2330004) 1-21, (2023).

[42] Mo., Sadique, Shah, S. R.,, "Mathematical model to study the effect of PRG4, hyaluronic acid and lubricin on squeeze film characteristics of diseased synovial joint", Int. J. of Mechanical Eng., 7 (6), 2022, 832-848.

[43] Purnima C., Shah, S. R., "Assessing the Clinical Outcomes of Voxelotor Treatment in Patients with Sickle Cell Disease", Int. J. of Applied Science and Biotechnology, 12(1), 46-53, (2024).

[44] Sadique, Mo., Shah, S. R.,, "Mathematical study for the synovial fluid flow in Osteoarthritic knee joint, Journal of Engineering and Applied Sciences, 17(2), (2022),15-21.

[45] Sapna, Siddiqui, S. U., "Study of blood flow through a stenosed capillary using Casson's fluid model", Ultra Science, Int. J of physical sciences, 16, (2)133-142, (2004).

[46] Shah, S. R., "A biomechanical approach for the study of deformation of red cells in narrow capillaries", IJE: Transaction A: Basics, 25(4), 303-313, (2012).

[47] Shah, S. R., "A biomechanical approach for the study of Two-phase blood flow through stenosed artery", Int. J. of research studies in biosciences, 1(2), 24-32, (2013).

[48] Shah, S. R., "A case study of non-Newtonian viscosity of blood through artherosclerotic artery", The cardiology, 6 (2),11-17, (2011).

[49] Shah, S. R., “A Mathematical Model for the analysis of blood flow through diseased blood vessels under the influence of porous parameter”, J. of Biosci. & Tech., 4(6), 534-541, (2013).

[50] Shah, S. R., “A mathematical study of blood flow through radially non-symmetric multiple stenosed arteries under the influence of magnetic field”, Int. J. of Advanced Research in Biological Sciences, 2 (12),379-386, (2015)

[51] Shah, S. R., “A mathematical study of blood flow through stenosed artery”, International Journal of Universal Science and Engineering, 1(1), 26-37, (2015).

[52] Shah, S. R., “A study of blood flow through multiple atherosclerotic arteries”, Int. J. for Math., 1, (12), 1-6, (2015).

[53] Shah, S. R., “A study of effects of magnetic field on modified Power-law fluid in modeled stenosed artery” Journal of Bioscience and Technology, 1 (4), 187-196, (2010).

[54] Shah, S. R., “An innovative solution for the problem of blood flow through stenosed artery using generalized bingham plastic fluid model”, Int. J. of research in applied and natural social sci., (2013) 1(3), 97-140.

[55] Shah, S. R., “An innovative study for non-Newtonian behavior of blood flow in stenosed artery using Herschel-Bulkely flud”, Int. J. of biosiences and biotechnology, 5(5), 233-240, (2013).

[56] Shah, S. R., “Capillary-tissue diffusion phenomena for blood flow through a stenosed artery using herschel-bulkley fluid” Int. J of Res. in Biochem. and Biophy.,1 (1).1-8 (2011).

[57] Shah, S. R., “Effect of clopidogrel on blood flow through stenosed artery under diseased condition”, Int. J. of Experimental Pharmacology, 4(1), 887-893, (2014).

[58] Shah, S. R., “Effects of Acetylsalicylic Acid on blood flow through an artery under Atherosclerotic condition”, Int. J.of Molecular medicine and advances sci. 7 (6),19-24, (2011).

[59] Shah, S. R., “Effects of antiplatelet drugs on blood flow through stenosed blood vessels”, Journal of Biomimetics, Biomaterials and Tissue Engineering, 18, 21-27, (2013).

[60] Shah, S. R., “Impact of radially non-symmetric multiple stenoses on blood flow through an artery”, International Journal of Physical and Social Sciences, 1 (3), 1-16, (2011).

[61] Shah, S. R., “Mathematical analysis of blood flow through atherosclerotic arterial segment having non-symmetric mild stenosis”. Int. J. of Rese. in Pure and Appl. Phy., (1) 1-5, (2011).

[62] Shah, S. R., “Mathematical Study of Blood Flow through Atherosclerotic Artery in the Presence of Porous Effect”, Int. J. of Modern Sciences and Eng. Tech., 2, (12),12-20, (2015).

[63] Shah, S. R., “Non-Newtonian flow of blood through an atherosclerotic artery”, Res. J. of Appl. Sci.6 (1),76-80, (2011).

[64] Shah, S. R., “Performance modeling and analysis of magnetic field on nutritional transport capillary tissue system using modified Herschel-Bulkely fluid”, Int. J. of Advanced research in physical sciences, 1(1).33-41, (2014).

[65] Shah, S. R., “Performance Study on Capillary-Tissue Diffusion Phenomena for Blood Flow through Stenosed Blood Vessels”, American J. of Pharmtech Res., 2(2),695-705, (2012).

[66] Shah, S. R., “Response of *blood flow through* an atherosclerotic *artery* in the presence of *magnetic field* using Bingham plastic fluid” Int. J. of Pha. & Biomed. Res.2(3),96-106, (2011).

[67] Shah, S. R., “Role of Non-Newtonian behavior in blood flow through normal and stenosed artery”, Research journal of Biological sciences, 6(9), 453-458, (2011).

[68] Shah, S. R., “Significance of Aspirin on Blood Flow to Prevent Blood Clotting through Inclined Multi-Stenosed Artery”, Letters In Health and Biological Sciences, 2(2), 97-100, (2017).

[69] Shah, S. R., “Study of dispersion of drug in blood flow with the impact of chemical reaction through stenosed artery”, International journal of Biosciences, 21 (3), 2022, 21-29.

[70] Shah, S. R., “Study of modified Casson’s fluid model in modeled normal and stenotic capillary-tissue diffusion phenomena” Int. J. of Comput. Eng. & Management. 11, 51-57, (2011).

[71] Shah, S. R., Akbar, S., “Mathematical Study for the Outflow of Aqueous Humor and Function in the Eye”, Int. Journal of Scientific & Engineering Research 11(10), 743-750, October-2020.

[72] Shah, S. R., and Anamika, “A mathematical model of blood flow through diseased blood vessel”, Int. J. of Emerging Trends and Tech. in Computer Science, 6, (3), 282-286, (2017).

[73] Shah, S.R., Clinical influence of hydroxychloroquine with azithromycin on blood flow through blood vessels for the prevention and Treatment of covid-19, Int. J. of biology, pharmacy and allied science, 10(7): 2195-2204.(2021).

[74] Sharma, S. K., Alshehri, Mo., Priya Gupta and Shah, S. R., “Empowering the visually impaired: Translating Handwritten Digits into Spoken Language with HRNN-GOA and Haralick Features”, J. of Disab. Res, 3, 1-21, (2024).

[75] Siddiqui, S. U., Shah, S. R., "A Physiologic Model for the problem of blood flow through Diseases blood vessels", Int. J of advances in Applied Sciences, 5(2), 58-64, (2016).

[76] Siddiqui, S. U., Shah, S. R., “Achievement of Pentoxifylline for Blood Flow through Stenosed Artery”, J. of Biomimetics, Biomaterials and Tissue Engineering, 13.81-89, (2012).

[77] Siddiqui, S. U., Shah, S. R., “Two-phase model for the study of blood flow through stenosed artery, International Journal of Pharmacy and Biological Sciences, 1(3), 246-254, (2011).

[78] Siddiqui, S. U., Shah, S. R., Geeta, “A Computational Analysis of a Two-Fluid non-Linear Mathematical model of pulsatile blood flow through Constricted Artery”, E-Journal of science and Technology, 10(4),65-78, (2015).

[79] Siddiqui, S. U., Shah, S. R.,“A Comparative Study for the Non-Newtonian Behaviour of Blood Flow through

Atherosclerotic Arterial Segment", Int. J. of Pharmaceutical Sci. Review and Res.,9 (2), 120-125, (2011).

[80] Siddiqui, S. U., Singh, A., Shah, S. R., "Mathematical Modeling of peristaltic blood flow through a vertical blood vessel using prandtl fluid model", Int. J. of Mathematics and Computer Research, 4, (9), 710-717, (2016).

[81] Singh, S., "A mathematical model for modified herschel-bulkley fluid in modeled stenosed artery under the effect of magnetic field", Int. J. of Bioeng. & Tech. 1 (1),37-42. (2010).

[82] Singh, S., "A two-layered model for the analysis of arterial rheology" International Journal of Computer Science and Information Technology, 4, 37-42. (2011).

[83] Singh, S., "Clinical significance of aspirin on blood flow through stenotic blood vessels" Journal of Biomimetics, Biomaterials and Tissue Engineering, 10, 17-24, (2011).

[84] Singh, S., "Effects of shape of stenosis on arterial rheology under the influence of applied magnetic field" Int. J. of Biomedical Eng. and Tech., 6 (3) 286-294, (2011).

[85] Singh, S., "Influence of magnetic field on blood flow through stenosed artery using casson's fluid model", Int. J. of BioEngineering, CardioPulmonary Sci. and Tech., 1,1-7, (2010).

[86] Singh, S., "Numerical modeling of two-layered micropolar fluid through a normal and stenosed artery", Int. J. Eng., 24 (2), 177-187, (2011).

[87] Singh, S., "Numerical modelling for the modified Power-law fluid in stenotic capillary-tissue diffusion phenomena", Archives of Applied Science Resaerch, *An Int. peer reviewed J. of appl. sci.*, 2 (1) 104-112, (2010).

[88] Singh, S., "The effect of Saline Water on viscosity of blood through stenosed blood vessels using Casson's fluid model", J. of Biomimetics, Biomaterials and Tissue Eng., .9 37-45, (2011).

[89] Singh, S., and Shah, R. R.,"A numerical model for the effect of stenosis shape on blood flow through an artery using power-law fluid", Advance in applied science research, *An Int. peer reviewed J. of Sci.*, 1, 66-73, (2010).

[90] Stiehl, T., Kumar, R., Shah, S. R., "Understanding the impact of feedback regulations on blood cell production and leukemia dynamics using model analysis and simulation of clinically relevant scenarios", Applied Mathematical Modelling, (2024).