UNSTEADY MATHEMATICAL ANALYSIS OF NON-NEWTONIAN BLOOD FLOW MODELS IN A DOUBLE STENOSED ARTERY

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DEDICATION

Special dedication to my parents for their love and encouragement. To my beloved husband and my children Rinad, Rama, Khalid and Faris for their patience and endurance for supporting me from the beginning to the end of my study – thank you for everything

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ABSTRACT

The simultaneous effect of pulsatile blood flow and double stenoses with different severities, lengths, and interspacing on mass transport using the Newtonian as well as the non-Newtonian power-law models of blood flow are considered in this thesis. These models are important from a physiological perspective as their effects on certain blood flow characteristics that are clinically significant can be analysed. The effect of some essential issues like the diffusivity of mass and the rate of absorption at the lumen-tissue interface are also studied to investigate the effectiveness of solute delivery. The flow is considered two-dimensional, unsteady and axisymmetric in the cylindrical polar coordinate system, while the transport of mass is modelled as an unsteady convection-diffusion equation. A numerical technique in the form of finite-difference approximations in staggered grids, widely known as the Marker and Cell (MAC) method has been used to tackle the coupled system of non-linear partial differential equations. Simultaneous effects of pulsatile flow conditions and double stenoses show an increase in the pressure drop across the stenosis length, as well as in the transport of mass at the throat and mass flux at the artery wall. The delivery of solute is observed to be more effective in the non-Newtonian model. In this study, another concern is on the effect of catheter's eccentricity on blood flow and heat transfer characteristics using the Carreau model. The perturbation method which is an approximate analytical technique, has been applied to the catheter problem. The accuracy of results is confirmed in the limiting cases, where the existing solutions in the literature are recovered as special cases. The position of the catheter's eccentricity in Carreau fluid leads to a reduction in the number and size of the circulating bolus zone which agree with physiological observations that the risks and complications associated with catheterization are alleviated when the eccentric position of the catheter is considered. The results of the simulation could provide insights towards the detection of aggregation sites, allowing the treatment of disease to be initiated quickly before it becomes clinically significant.

ABSTRAK

Kesan serentak aliran darah berdenyut dan stenosis berganda dengan tahap keparahan, panjang, dan jarak yang berbeza terhadap pengangkutan jisim menggunakan model aliran darah Newtonan dan tak-Newtonan hukum kuasa dipertimbangkan di dalam tesis ini. Model-model ini penting dari perspektif fisiologi kerana kesannya terhadap beberapa ciri aliran darah tertentu yang signifikan secara klinikal dapat dianalisis. Kesan daripada beberapa isu utama seperti penyebaran jisim dan kadar penyerapan di kawasan antara-muka tisu-lumen juga dikaji untuk menguji keberkesanan pengangkutan bahan terlarut. Model aliran bendalir dianggap dua dimensi, tak mantap dan simetri sepaksi dalam sistem koordinat silinder, sementara pengangkutan jisim dimodelkan sebagai persamaan perolakan-penyebaran tak mantap. Teknik berangka dalam bentuk penghampiran perbezaan terhingga dengan grid berperingkat, yang lebih dikenali sebagai kaedah Marker dan Cell (MAC) telah digunakan untuk menyelesaikan sistem persamaan pembezaan separa tak linear. Kesan gabungan antara aliran berdenyut dengan stenosis berganda menunjukkan peningkatan dalam tahap penurunan tekanan di sepanjang stenosis, serta pengangkutan jisim di kawasan kerongkong dan fluks jisim di dinding arteri. Pengangkutan bahan terlarut diperhatikan lebih berkesan bagi model tak-Newtonan. Di dalam kajian ini, satu lagi permerhatian adalah kepada kesan eksentrik kateter terhadap aliran darah dan ciri pemindahan haba menggunakan model Carreau. Kaedah usikan yang merupakan suatu kaedah analisis penghampiran, telah diterapkan pada masalah kateter. Ketepatan hasilnya disahkan dalam kes-kes penghad, di mana hasil kajian yang terdapat di dalam literatur diperoleh sebagai kes khas. Kedudukan eksentrik kateter dalam bendalir Carreau menyebabkan bilangan dan saiz zon bolus yang beredar berkurang, dengan menepati pemerhatian fisiologi bahawa risiko dan komplikasi yang berkaitan dengan kateter dapat dikurangkan ketika kateter berada pada kedudukan eksentrik. Hasil simulasi dijangka dapat mengesan situs agregasi yang membolehkan rawatan segera di ambil sebelum sesuatu penyakit itu dikesan secara klinikal.

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LIST OF ABBREVIATIONS

CVD	-	Cardiovascular Disease
CFD	-	Computational Fluid Dynamics
ECs	-	Endothelial Cells
LDL	-	Low-Density Lipoprotein
MAC	-	Marker and Cell Method
PK	-	Pharmacokinetics
RBCs	-	Red Blood Cells
SMCs	-	Smooth Muscle Cells
SOR	-	Successive Over Relaxation Method
WSS	-	Wall Shear Stress
WBCs	-	White Blood Cells

LIST OF SYMBOLS

$\mathbf{F}$	-	Body forces
$\boldsymbol{D}$	-	Rate of strain tensor
$\mathbf{V}$	-	Velocity vector
u	-	Velocity component in radial direction
w	-	Velocity component in axial direction
v	-	Velocity component in theta direction
V_0	-	Velocity of catheter
U_0	-	The cross-sectional average velocity
C_i	-	Mass concentration, $i = l$ for lumen, $i = t$ for tissue
C_s	-	The reference concentration at the inlet
c_p	-	Specific heat
D_i	-	Coefficient of mass diffusion, $i = l$ for lumen and $i = t$ for tissue
T	-	Blood temperature
T_0	-	The respective temperature at the inner wall
T_1	-	The respective temperature at the arterial wall
K_c	-	Reaction rate constant
L	-	Total length of arterial segment
R_i	-	Radius of the arterial segment in the stenotic region, $i = 1$ double stenoses and $i = 3$ overlapping stenosis
R_0	-	Radius of the annular region in the non-stenotic artery
Re	-	Reynolds number
Sc	-	Schmidt number
$\mathrm{Pe_i}$	-	Peclet number, $i = l$ for lumen and $i = t$ for tissue
$\mathrm{Sh_D}$	-	Sherwood number
We	-	Weissenberg number
Pr	-	Prandtl number
Ec	-	Eckert number

$\mathrm{Nu}_{\mathrm{ave}}$	-	The mean Nusselt number
m	-	Consistency factor
n	-	Flow behavior index
p	-	Pressure
α	-	Womersley number
η	-	The wall absorption parameter
Δt	-	Time increment
Δx	-	Increment in the radial direction
Δz	-	Increment in the axial direction
ρ	-	Density of blood
$\boldsymbol{\tau}$	-	Stress tensor
μ_{app}	-	Non-Newtonian viscosity
σ	-	Catheter radius
ϵ	-	Eccentricity parameter
β	-	Combination factor
κ	-	Thermal conductivity
Γ	-	Time constant
μ	-	Constant viscosity
μ_∞	-	Infinite shear rate viscosity
μ_0	-	Zero shear rate viscosity
λ	-	Impedance to flow
ω	-	Angular frequency
ω_0	-	Over relaxation parameter
ω_u	-	Under relaxation parameter
θ	-	Angle of circumferential direction
δ	-	Critical height of stenosis

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CHAPTER 1

INTRODUCTION

1.1 Research Background

Stenosis is the narrowing or restriction of blood vessel or valve that reduces blood flow. For example, aortic stenosis is the aortic valve in the heart. This narrowing often causes a sharp increase in the resistance to flow through the vessels. Over time, stenosis can advance to a complete blockage of the artery (Young (1968)). It affects the velocity of blood flowing through the artery, affecting blood pressure and may cause the heart to collapse. The damage caused to the heart or blood vessels can cause cardiovascular disease (CVD). Examples of CVD are coronary artery and carotid artery diseases. In coronary artery disease, a plaque buildup occurs in the arteries of the heart and can cause a heart attack while carotid artery disease can cause stroke (Ougrinovskaia *et al.* (2010)).

The narrowing usually results from atherosclerosis, which refers to a build-up of plaque on the inside of the arteries. The process of build up is call artherogenesis. The artery walls are normally smooth to allow blood flow easily through the artery and for easy transportation of mass or atherogenic particles such as fat, cholesterol which exists in blood in the form of low-density lipoproteins (LDL), calcium, and other substances within the artery wall. When the plaque is brittle and ruptures the most serious harm takes place in which the tear of plaque causes blood clots which could block the arterial lumen and/or move to another part of the circulatory system, which are eventually responsible for strokes, and heart attacks, difficulty in walking and gangrene (Thubrikar (2007)). Atherosclerosis is the major cause of CVD and remains the leading factor of death. Ross (1999) wrote that atherosclerosis is an inflammatory disease, in which high concentrations of cholesterol in the blood is one of the principal risk factors.

Caro *et al.* (1971) reported that atherosclerosis (see Figure (1.1)) may occur based on shear-dependent mass transfer mechanism between blood cholesterol and the arterial wall. Caro and Nerem (1973) noted that the correlations between shear stress and atherosclerosis may be due to the alteration in convection mass transfer since the mass transfer due to convection depends on the velocity gradient, which is related to shear stress. This means the balance between convection and diffusion in the bloodstream and arterial wall determines which molecules enter, exit and remain entrapped (Fry (1987)). In order to make an appropriate assessment regarding the possible relationship between the spots of atherosclerotic lesions and the mass transfer patterns, an accurate characterization of mass transport behavior is very important. Moreover, a clear knowledge of mass transfer in a stenosed artery is of considerable medical interest in the formation and development of atherosclerosis.

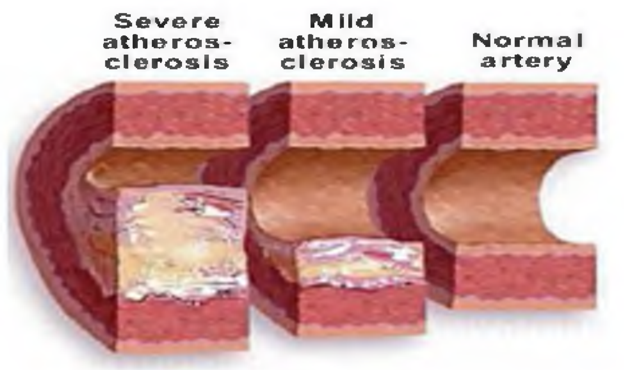

Figure 1.1: Progression of atherosclerosis (https://www.newbeginningshealthcare.net/blog/what-is-atherosclerosis).

The study of blood rheology and the dynamical characteristics of its flow is a very important step towards the comprehension, prediction, diagnosis, and therapy of CVD. Blood is a complex and exhibits various types of rheology behavior depending on the size of the vessel in a specific location. From a biofluid mechanics point of view, blood would not be expected to obey the very simple, one parameter, and linearized law of viscosity as developed by Newton (Mustapha and Amin (2008)).

However, CVD usually develops over a long time, thus it can be prevented or delayed by effectively managing and modifiable risk factors. Corrective therapies involve drug regimens and various forms of surgical intervention. The delivery of a solute from the bloodstream to the site of drug action primarily depends on blood flow but blood flow to different organs of the body is not equal. The effect of some essential issues like the diffusivity of mass, the rate of its absorption at the lumen-tissue interface with the flowing blood are important to analyze.

In some instances, surgery may be necessary to treat clogged arteries and prevent arterial plaque accumulation. The most common surgical intervention is artery catheterization and it is a quick procedure involving minimal risk while in more severe cases coronary bypass is used. Artery catheterization is the insertion of small plastic tubes (catheters) into arteries and veins (see Figure (1.2)) to the heart to obtain x-ray pictures (angiography) of coronary arteries, to determine whether blood vessels supplying the heart muscle are obstructed and to measure pressures and flow velocity or flow rate in the heart (hemodynamics). The transportation of drug or its delivery also involves a catheter being inserted into the artery.

Figure 1.2: Arterial catheter (https://www.medline.com/product/Arterial-Catheters/Kits-by-Argon-Medical/Z05-PF27732).

The procedure involving catheter brings about potential complications which may include reaction to sedation, infection, and bleeding. When a catheter is inserted into the artery, it creates an annular region between the walls of the catheter and artery. Insertion of catheter further increases impedance frictional resistance to flow that would change the flow characteristics such as velocity, pressure, and streamlines (Dash *et al.* (1996)).

Blood does not only transport metabolites, oxygen and other dissolved substances to and from the tissues, but it also alters heat transfer or the transport of heat within the body. This is to meet the changing demands of the organism whose cardiovascular system for example, is sensitive to changes in the environment such as temperature change. In biological systems, it is very important to consider the variation of temperature because a slight change in temperature, for example, if the temperature of human blood rises above $1°C$, irreversible harm occurs in the blood proteins (Quast and Kimberger (2014)).

Over the years, many mathematical models have been developed to study blood flow. These mathematical models are being continuously improved and upgraded to take into account more realistic physical conditions. The solution to these problems involve complex mathematical equations which are difficult to solve and most solutions obtained involved numerical methods. Analytical methods can only be approached in special cases when the equations are very much simplified. In this thesis, four different situations based on the research background above are analysed to study the effect of boundary conditions, the type of fluid , the effect of certain parameter on mass transport at the lumen-artery interface and the effect of catheter insertion on heat transfer, with specific problem statements and research questions as outlined in Section 1.2.

1.2 Problem Statement

Most mathematical models to investigate mass transfer in stenosed artery assume the artery to have a single mild stenosis, the artery wall is rigid, the flow is time independent and the inlet velocity is parabolic. In real situation, the patient is found to have multiple stenoses in the same arterial segment, the arterial blood flow is unsteady and the effect of the unsteadiness on pressure drop is important and flow from the heart comes from a large pressure reservoir into successively smaller tubes resulting in pulsatile velocity at the inlet region. The first research question is how are the blood flow and mass transfer characteristics altered when flow pulsatility and double stenoses are considered simultaneously.

The next problem is concerned with the nature of blood itself. Experimental investigations have revealed that blood exhibits non-Newtonian properties at low shear rate. The non- Newtonian behavior of blood is most evident in small vessels or at very low shear rates (Tu and Deville (1996)). Since the shear rate is low in the downstream of the stenosis, a correct analysis of the flow pattern should include the non-Newtonian factor. The question then is how the non-Newtonian model of blood flow affects the characteristics of flow and mass transport in an artery with double stenoses and pulsatile inlet condition.

Where mass transfer is concerned, the majority of works on mass or solute transport were performed by considering tubular geometrical model with thin boundary and the analysis was restricted to the solute dispersion in the fluid phase of the tube only. In reality, the arterial wall is thick and mass is transported via a number of realistic lumen-tissue interface conditions, thus the unsteady coupled problem interconnecting the dispersion of mass from lumen into tissue must be taken into consideration. The interphase mass transfer due to the absorption at the tube wall plays an important role on the dispersion process of solute. This phenomenon has lots of applications in hemodynamics for permeable blood vessels, tubular flow reactors with heterogeneous catalysis, bioengineering (haemodialysers and oxygenators) and physiology. Applications in which absorptive wall is also of major importance include tubular flow reactors and soluble gas uptake by the walls of pulmonary airways, and is of particular significance in the mixing and the transportation of drugs or toxins in physiological systems. Since the therapeutic domain for atherosclerotic disease is the stenosed arterial wall and for the better treatment of the patient, study the uptake of an injected drug under various luminal conditions at the absorptive lumen-tissue interface and its subsequent dispersion into the arterial wall is an important consideration because it closely resembles the physiological situation concerning intravenous drug delivery. The research question here is how the absorptive wall affects the diffusivity of mass within lumen and the arterial tissue.

In the course of drug transport or delivery, where the insertion of a catheter is concerned, the catheter is usually placed in an eccentric position, one reason being to reduce pain in the patient. However, most analysis involving catheterized flow considered that the catheter to be in concentric position. But a more realistic condition is that the catheter is usually placed in an eccentric position, one reason being to reduce pain. Another condition to consider is a mathematical model that takes into account temperature change as it is common knowledge that a temperature rise of merely $1°C$ or $2°C$ for example would cause a fever. A more realistic flow model should include the energy equation. The research question here is how the eccentric catheter affects blood flow characteristics when temperature is taken into account.

1.3 Research Objectives

The main objective of this research is to carry out a mathematical analysis using both analytical and numerical means to investigate the effects of different boundary conditions and flow domains on the flow, mass transport and heat transfer characteristics of blood in a stenosed artery.

Specific objectives are:

(a) To determine the simultaneous effect of pulsatile blood flow and double stenoses on mass transport.
(b) To analyze the effects of power-law model of blood flow and pulsatile inlet on mass transfer in an artery with double stenoses.
(c) To calculate the distribution of mass from lumen to tissue through a stenosed artery in the presence of absorption at the tube wall.
(d) To determine the effects of eccentric catheterization on Carreau model of blood flow with heat transfer in an overlapping stenosed artery.

1.4 Scope of the Study

This research takes into consideration blood flow through a double stenosed artery with pulsatile boundary condition. The geometry of stenosis considered is the double and overlapping one. The fluid is assumed to be incompressible where only the Newtonian and non-Newtonian models of blood characterized by the power-law model and Carreau model are considered. The flow is assumed laminar, two-dimensional axisymmetric in the cylindrical coordinate system. For the solution procedure, the analytical technique is the perturbation method with mild condition approximation while the numerical technique is the finite difference the Marker and Cell (MAC) method. Simulations are carried out using published data in the literature.

1.5 Significance of Research

Mathematical models of blood flow in the cardiovascular system provide insight into normal and diseased conditions in blood vessels and have applications in areas such as surgical planning and designs of medical devices. A mathematical analysis on the flow characteristics of blood with the consideration of the real situation could make it possible to predict whether the problems faced by patients need medical intervention in the form of invasive surgery or otherwise. For example in CVD, the cardiologist needs to determine whether the patient need a bypass or not based mostly on his experience. This is very risky for the patient if the doctor is inexperienced.

On the other hand, with mathematical analysis possible complications could be determined non-invasively and cheaply without unnecessary complications. In the present work, if the geometry of stenosis of a cardiac patient could be obtained through angiograms, the flow characteristics namely the wall shear stress, the pressure drop and the streamlines could be calculated and a suitable range of values that cause complications could be established.

Specifically in this project, the critical length of stenoses , severity etc could determine whether they affect mass transport, whether recirculations have occurred and so on. Further, it provides information on how absorption affects mass transport at the lumen, how catheter position, size and velocity of insertion affects the artery, thus enabling medical practitioners to choose a suitable catheter for insertion, and by how much it should expand an artery. If a catheter is not expanded enough it will not be doing its job, but if it is expanded too much it can risk damaging the artery. Most importantly, with sufficient statistical data, mathematical analysis has the ability to predict various flow characteristics that could be used for validation purposes with experimental and clinical results.

Mathematical analysis could significantly reduce the cost of diagnosing and treating a disease. It could be expected to minimize physiological through non-invasive procedure psychological stress and cost of treatment on patients. For manufacturers of products and regulators, mathematical analysis can be the mechanism that supports efficient review of novel products and approaches without compromising on safety and effectiveness.

1.6 Thesis Organization

This thesis is comprising of eight chapters as given below: Chapter 1 starts with the research background which outlines the general introduction followed by problem statement, research objectives, scope and significance of the study.

In Chapter 2, a literature review with respect to the issues sketched out within the problems outlined in the objectives is displayed and discussed in detail.

In Chapter 3, the differential form of the equations and the mathematical model that governed the flow namely Newtonian, power-law and Carreau models are presented. This chapter starts with the conservation of mass, momentum, mass and energy equations. It then follows with the discussion about the appropriate boundary conditions.

In Chapter 4, the first problem which looked at the numerical investigation to determine the effect of severity, the distance between double narrowings and flow pulsatility on the transport of blood and mass. This chapter is divided into six main sections including the introduction, governing equations, solution procedure, stability and accuracy, numerical algorithm and numerical results and discussion.

Chapter 5, accounts for shear-thinning model of blood flow, known as power-law model through a double stenosed artery to improve the previous chapter by considering the non-Newtonian nature of blood.

Chapter 6, addresses the distribution of mass in a stenosed arterial segment as well as in the tissue with the streaming blood represented by the power-law model. The coupled system of non-linear mass and momentum transport along with appropriate boundary conditions is solved numerically using the finite difference scheme MAC method.

In Chapter 7, describes the effect of catheter insertion on blood flow and heat transfer characteristics of a Carreau fluid model by using the perturbation method involving two appropriate small parameters. Finally, in chapter 8 concludes the thesis together with useful suggestions and recommendations for pursuing future research.

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