



School of Pure and Applied Sciences
Department of Mathematics & Statistical Sciences

**MAGNETIC DRUG TARGETING PHENOMENA DURING NON-
NEWTONIAN FLOW IN THE MICROVESSEL WITH TIME-
FRACTIONAL DERIVATIVE**

by

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A Thesis Submitted to the School of Pure and Applied Sciences in Partial Fulfillment of the
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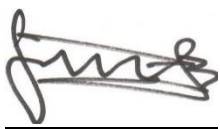
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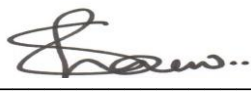
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Abstract

Cancer and cardiovascular disease are the leading causes of death worldwide incurring substantial medical costs and care and become a potential barrier to average life expectancy. Several treatment options available have considerable side effects and often are not sufficient for curative treatment. Most challenges include targeting non-specifically, poor pharmacokinetic characteristics drugs arising from poor solubility, stability, and toxicity, inefficacy and limited bio-distribution. Recently, with the advancement of nanotechnology, treatment options such as magnetic drug targeting (MDT) through the application of magnetic nanoparticles (MNPs) treatment have significantly changed the paradigm of cancer treatment due to minimum side effects and high efficacy. This research aims at theoretical analysis to examine the efficacy of the accumulation of drug carrier magnetic nanoparticles influenced by biophysical parameters near the diseased region during magnetic drug targeting.

In this study, the time fractional derivatives of blood flow and factors governing the transport of drug carrier nanoparticles such as particle – particle interaction, Saffman uplift force, size and shape of carrier particles, permeability of the vessel, magnetic and viscous forces are considered. The conclusion drawn from the study shows that spherical shaped drugs carrying magnetic nanoparticles are more prominent to be targeted to the tumor region than other non-spherical shaped drugs carrying magnetic nanoparticles. Capture efficiency of the drug-carrier particles is improved with increase in the magnetization, and radius of carrier particles as both increase the magnetic force among the magnet and Drug-carrier particles. A decrease in Darcy number, Reynolds number, and tumor magnet distance decreases the total volume fraction of nanoparticles. Total volume fraction of magnetic nanoparticles decreases with increase in pulsatile frequency, Casson parameter and Hematocrit parameter. The velocity of blood and velocity of magnetic nanoparticles are boosted with enhancement in the Darcy number and Jeffrey fluid parameter, which shows an important application to the therapy of atherosclerosis. The flow resistance increases with an increase in stenosis height and Hartman number. The present study will help biomedical engineers and nanomedicine researchers develop magnetic devices and the next generation of drug carrier particles to treat cancerous tumors.

Key words: Magnetic drug targeting, Fractional derivative, Drug – carrier particles, Magnetic nanoparticles, tumor.

Nomenclature

g	Acceleration due to gravity (m/s^2)
A_0	Body acceleration amplitude (m/s^2)
ℓ_0	Body acceleration amplitude (m/s^2)
b_0	Pressure gradient amplitude (Pa/m)
b_1	Pulsatile element amplitude (Pa/m)
q_1	Transient part amplitude (Pa/m)
B_0	Applied magnetic field (T)
H_a	Applied magnetic field intensity at the center (T)
M_m	Average mass of magnetic nanoparticles (kg)
D_v	Vessel diameter in microns (m)
k	Body acceleration frequency (Hz)
R_{cp}	Carrier particle's radius (m)
W_{CP}	Carrier particle's volume (m^3)
M_0	Characteristic magnetization parameter (A/m)
u_0	Characteristic velocity (m/s)
Da	Darcy number
D_v	Diameter of the blood vessel in micron (m)
C_D	Drag coefficient
A_{CP}	Drug carrier's cross-sectional area (m^2)
E	Electric field (N/C)
S_{rz}	Extra tensor of the Jeffrey fluid
V_{avg}	Fluid's average velocity (m/s)

F_f	Fluidic force (N)
F_f	Fluidic force (N)
f_b	Frequency (Hz)
f_b	Frequency (Hz)
Ha	Hartmann number
M	Hartmann number
H_D	Hematocrit of blood
H_D	Hematocrit parameter
b_0	Induced magnetic field (T)
L_{mv}	Length of microvessel (m)
d	Location of the stenosis (m)
B	Magnetic flux intensity (T)
F_m	Magnetic force (N)
V_{mp}	Magnetic nanoparticle's volume (m^3)
M_s	Magnetization parameter (A/m)
p_m	Mass parameter of particles
δ	Maximum height of the stenosis (m)
u_f	Mean velocity of fluid (m/s)
J	Current density (A/m^2)
N	Number of magnetic nanoparticles per unit volume
pc	Particles concentration parameter
m_{cp}	Particles mass (Kg)
k_p	Permeability of the porous medium (H/m)
h_0	Pressure gradient's amplitude (Pa/m)
h_1	Pulsatile element amplitude (Pa/m)

u_r	Radial velocity of blood (m/s)
R_{cp}	Radius of carrier particles (m)
R_{mag}	Radius of cylindrical magnet (m)
R_{mp}	Radius nanoparticles (m)
R_{mv}	Radius of microvessel (m)
R	Radius of stenosis (m)
Re	Reynolds number
F_s	Saffman force (N)
S	Saffman force parameter
k'	Shape factor
q_0	Steady amplitude (Pa/m)
L_0	Stenosis length (m)
w	Stenosis shape parameter
k	Stoke's constant (N-s/m ²)
K_s	Stoke's constant (N-s/m ²)
D_p	Suspended particle's diameter (m)
d_{vm}	Tumor-magnet distance (m)
V	Velocity vector (m/s)
u	Velocity of fluid (m/s)
v	Velocity of magnetic nanoparticles (m/s)
V_{mp}	Volume of magnetic nanoparticles (m ³)

Greek symbols

ρ	Density of magnetic nanoparticles (kg/m ³)
γ_0	Difference with the pulsatile pressure gradient
λ_1	Ratio between relaxation and retardation times

λ_2	Retardation time (s)
μ_0	Air permeability (H/m)
μ_{bf}	Base fluid viscosity (N.s/m ²)
χ	Cylindrical drug carrier's aspect ratio
σ	Electrical conductivity (S/m)
γ	Fluid shear rate (1/s)
α	Fractional parameter
ν	Kinematic viscosity (m ² /s)
μ_{nf}	Nanofluid viscosity (N.s/m ²)
v_{cp}	Particle's velocity (m/s)
ϕ	Particle's volume fraction
μ_{plasma}	Plasma viscosity (N.s/m ²)
γ	Prolate ellipsoidal drug carrier's aspect ratio
ω	Rotational frequency (Hz)
λ	Relaxation time parameter of Maxwell fluid (s)
$\beta_{vf,100}$	Total volume fraction of magnetic nanoparticles

Dedications

Dedicated to my beloved parents.

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List of Publications

[1] **H. B. Yadeta**, S. Shaw, Contribution of rational design and fractional rheology on magnetic nanoparticle-based drug targeting in a microvessel with Saffman force, *Chin. J. Phys.* **87** (2024) 677–696.

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1. Introduction

1.1. Background

Cancer and cardiovascular disease are the leading causes of death worldwide incurring substantial medical costs and care. Cancer is a collection of related diseases where some cells divide without stopping and spread into surrounding tissues. Cancer can start almost anywhere in the body. Normally, our cells grow and divide to form new cells, as our body needs them. When a cell grows, gets old or becomes damaged, they die, and new cells take their place. When cancer develops, however, this orderly process breaks down. Cells become more and more abnormal. Old or damaged cells survive when they should die, and new cells form when they are not needed. These extra cells can form growths called tumors. Cancerous tumors are malignant, which means they can invade nearby tissues. In addition, as these tumors grow, some cancer cells can break off and travel to distant places in the body through the blood or the lymph system and form new tumors far from the original (which is called metastatic condition) [1]. Solid tumors are masses of tissue named for the type of cells they formed from. Liquid tumors, such as leukemias, are cancers of the blood and bone marrow. Unlike malignant tumors, benign tumors do not spread into nearby tissues and often do not grow back when they are removed. Benign tumors can sometimes be quite large and, in the case of benign brain tumors, can be life threatening [1].

Nowadays, cancer is among the leading causes of death worldwide and is an important barrier to increasing average life expectancy. Globally, 19.3 million new cases and 10.0 million cancer-related deaths occurred in 2020 [2]. Overall, the burden of cancer incidence and mortality is rapidly growing world-wide; this reflects both aging and growth of the population as well as changes in the prevalence and distribution of the main risk factors for cancer, several of which are associated with exposure to chemicals, age and family history, tobacco, radiation, obesity [3, 4].

There are several cancer treatment options available, each therapy depends upon the type of cancer, grade, and stage. In recent decades, chemotherapy, surgery, and radiotherapy have been used to treat different types of cancer. Most chemotherapy treatments are administered intravenously. Chemotherapy may be given by mouth, injection, or infusion, or on the skin, depending on the type and stage of the cancer being treated. Tumor surgery is an operation or procedure to remove

the tumor and possibly some surrounding tissues. Radiotherapy uses energy beams (gamma rays, x-rays, protons, or electron beams) for targeting cancer cells or tumors. However, all these procedures have considerable side effects and often are not sufficient for the curative treatment of metastatic cancer [5, 6]. Most challenges include targeting non-specifically any rapidly dividing cells irrespective of whether they are tumorous or not, poor pharmacokinetic characteristics of anticancer drugs arising from poor solubility, stability, and metabolism pose different challenges of toxicity, inefficacy and limited bio-distribution. Recently, with the advancement of nanotechnology, a treatment option that can effectively address the above cited challenges and provide selective targeting of tumor sites without significant damage to the viability of healthy tissues has been developed [7–13]. The emerging alternative of nanotechnology presents a new frontier in cancer treatment [14]. Early research on the therapeutic application of nanoparticle carriers as a drug delivery system has been highly encouraging. Progressively, research explores the use of magnetic drug targeting through the application of magnetic nanoparticle treatment strategies due to high efficacy and minimum side effects [15].

1.1.1. Cardiovascular disease

The cardiovascular system's primary job is to deliver nutrients throughout the body and remove the wastages and toxins from the body. Additionally, the cardiovascular system provides the body with a defense mechanism against infections and illnesses. It also aids in the regulation of temperature and fluid balance throughout the body [16, 17]. Cardiovascular disease (CVD) includes a range of disorders that affect both the heart and blood vessels and is the leading cause of mortality globally [18]. The main cause of cardiovascular disease is the formation of atherosclerotic plaque, a build-up of fatty material in the arterial wall. When plaque build-up, it blocks the blood supply, it can ultimately result in a range of conditions, such as coronary artery disease, cerebrovascular disease, and peripheral artery disease [19, 20].

The major contributing factor in many cases of cardiovascular disease and cerebra-vascular disease (stroke) is atherosclerosis. One of the outcomes of this disease process is the narrowing of the arteries resulting from sub-endothelial deposition of cholesterol, cholesterol esters, and calcium within the vessel walls. These cholesterol-rich plaques also contain a variety of cell types, including fibroblasts and immune cells [21]. Rupture of the atherosclerotic plaques yield thrombi that travel distally to occlude the artery, resulting in myocardial infarction or stroke. Several factors

increase the risk for atherosclerosis including a predisposition for elevated levels of cholesterol and triglyceride in the blood; high blood pressure; diabetes; and cigarette smoking. Normal cells obtain most of the cholesterol they need for normal functioning by taking up cholesterol from the blood through receptor mediated endocytosis. Cholesterol is transported in the blood bound to low-density lipoproteins. Cholesterol uptake is blocked in some people, and excess cholesterol accumulates in the blood to eventually form atherosclerotic plaques. If these plaques occlude blood flow in brain arteries, the result can be stroke; if they occur in coronary arteries, it can lead to myocardial infarction [22].

There are several treatment mechanisms for atherosclerosis such as surgical intervention for advanced cases, invasive procedures, such as coronary artery bypass grafting and carotid endarterectomy, and non-surgical procedures such as percutaneous coronary intervention, which contain several risks such as restenosis and in stent restenosis. Treating cardiovascular disease remains a significant challenge, primarily because of low drug accumulation at the disease site. Treatment of this condition necessitates high and prolonged drug dosages that often lead to severe adverse effects [23]. Limitations in cardiovascular disease therapeutic and diagnostic landscapes have generated excitement for advances in nanomedicine, a field focused on improving patient outcomes through transformative therapies, imaging agents and ex vivo diagnostics [24]. Magnetic nanoparticle-based drug targeting represents an efficient platform to deliver drugs to diseased arteries in vivo [24].

1.1.2. Magnetic drug targeting

Drug targeting is a principle by which the transport of a drug in the organism is maneuvered in a manner such that its major fraction interacts exclusively with the target tissue at the cellular or subcellular level. Magnetically controlled drug targeting is one of the various possibilities of drug targeting. This technology uses the binding between anticancer drugs and a Ferrofluid to concentrate the drug in an area of interest [25]. Super paramagnetic iron oxide nanoparticles are frequently used in medical research for new drug carriers (Fe_3O_4). These particles are biodegradable, and they are still in use as a contrast agent in magnetic resonance imaging. Magnetic drug targeting is a promising attempt for treating tumors and arterial disease. This method applies super paramagnetic nanoparticles bound to chemotherapeutics and injected into the supplying vascular system of the respective tumor while focused by a strong external magnetic

field to selectively target this region. This leads to higher doses of the chemotherapeutic agent in the tumor region with a reduced overall dose [26] (see Figure 1.1).

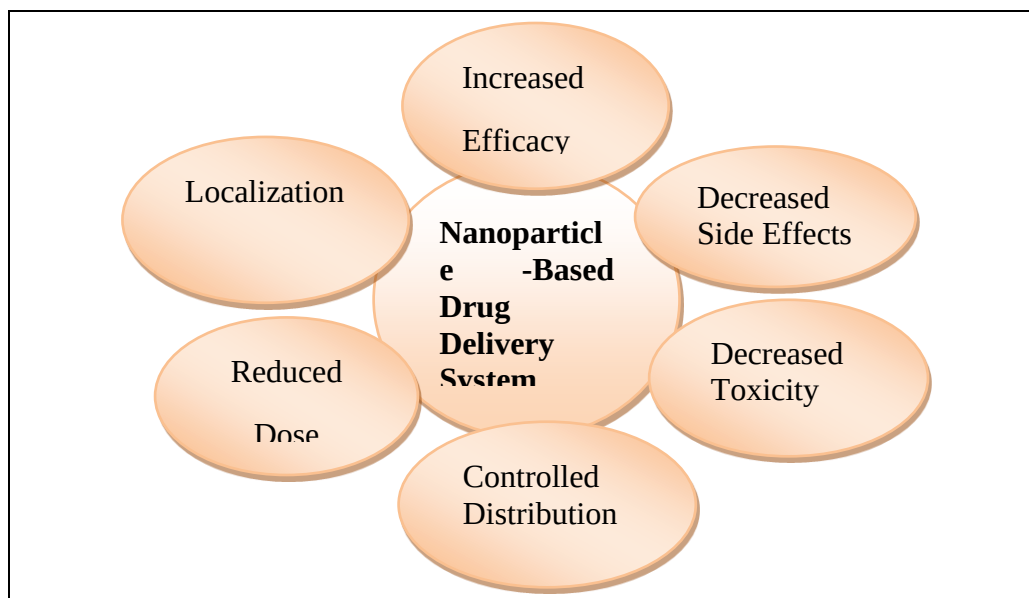


Figure 1.1 Ideal characteristics of nanoparticle-based targeted drug delivery system in microvessel [35].

In addition to the magnetic field that significantly affects the trajectories of drug carrier magnetic nanoparticles, there are also certain factors that affect the efficacy of the trajectories of the particles during drug targeting. Such factors include the rheology of the blood, the shape and size of drug carrier magnetic nanoparticles, the permeability of the blood vessel wall, the uplift force, and others. The shape of drug carrier magnetic nanoparticles performs a significant function in drug loading and release, biocompatibility, circulation time, targeting, and subcellular adoption. In recent developments, different shapes of drug carrier particles have been developed. Because of their symmetric nature and the presence of well-defined models of hydrodynamic interactions [27], and thermodynamic favorability [28] spherical drug carrier magnetic nanoparticles are widely used in drug delivery. Subject on the size and shape of the cells or organs, non-spherical drug carrier magnetic nanoparticles, such as ellipsoids, cylinders, cones, discs, and biconcave discoids [29 – 31], ellipsoidal (oblate, and prolate) [32], are applicable in various areas of the organs. However, the use of non-spherical drug carrier magnetic nanoparticles for drug delivery is limited due to a

lack of techniques to fabricate non-spherical biocompatible carriers [33]. Despite the inadequate availability of non-spherical carrier particles, carrier shape has a significant effect on cellular internalization, margination towards the target region, and trajectories towards the tumor region [34].

1.2. Statement of the problem

Cancer and cardiovascular disease are global chronic diseases with a high mortality rate, and the availability of more precise and effective treatments is imminent. Currently, available treatment options for cancer include surgical therapy, radiation therapy, and systemic therapy [36, 37]. However, systemic therapy is the only possible treatment option for metastatic cancer. Among systemic therapies, chemotherapy is the most used; however, conventional chemotherapy is often associated with issues such as non-selectivity, toxic side effects, and insufficient drug doses at the therapeutic site, which decreases the efficiency of treatment. Diagnosing cardiovascular disease involves a comprehensive approach, incorporating techniques such as echocardiography [38], electrocardiography [39], computed tomography [40], and magnetic resonance imaging [41]. Surgical procedures play a pivotal role in addressing specific cardiovascular diseases [42]. Pharmacotherapy constitutes a crucial element in cardiovascular disease treatment, with various drug classes like anticoagulants, antiplatelet agents, ACE inhibitors, beta-blockers, and statins commonly employed [43]. However, these established treatments may have limitations, including adverse reactions [44]. On the other hand, several cancer treatment procedures available have considerable side effects and often are not sufficient for the curative treatment [5]. The aforementioned limitations in cancer and cardiovascular disease (in particular atherosclerosis) treatment can be overcome by the means of magnetic drug targeting delivery system, which delivers the drug directly to the desired site cells, thereby minimizing the off-target, toxicity effects while concentrating the drug at the target site with the help of suitable drug carriers.

1.3. Aims and objectives

This research work aims to understand, extend the existing models of blood flow with drug-carrying magnetic nanoparticles, reformulate and solve them, and know the capture efficiency of

carrier particles in the diseased region during magnetic drug targeting. To achieve this desired aim, the objectives of the present study are to:

1. apply the semi-analytic approach to solve the governing time fractional mathematical models of blood flow in the microvessel.
2. examine the capture efficacy of drug carrier magnetic nanoparticles in the diseased region.
3. describe the effects of biophysical parameters on the trajectories and distribution of carrier particles.
4. examine the impact of memory effects during magnetic drug targeting.

1.4. Structure of the thesis

This section contains a summary of how this thesis is organized. The thesis consists of seven chapters.

Chapter 1 deals with a general introduction related to cancer, cardiovascular disease, and the magnetic drug targeting concept. Further, this chapter introduces the statement of the problem and the aims and objectives of the thesis.

In chapter 2, we give a review of the literature related to the research work consisting of governing equations of fluid motion (Navier-Stoke's equations) and the rheology of non-Newtonian fluids.

Chapter 3 is concerned with mathematical concepts, definitions, integral transforms, and special functions that are used throughout the thesis to aid us in obtaining mechanisms to find solutions to the governing equations.

In chapter 4, we present the analysis of the axial trajectories of drug-carrier magnetic nanoparticles towards the tumor region in an axisymmetric microvessel. The transport of these particles is governed by several factors; we have only considered the dominant factors such as magnetic force, viscous drag force (fluidic force), particle-particle interaction, and Saffman uplift force. The governing equation of blood flow is represented by the Caputo-Fabrizio time fractional derivative model to consider the non-local nature of the memory effect.

In Chapter 5, magnetic drug targeting during Casson blood flow in a microvessel with a Caputo time fractional derivative is presented. The study focuses on the analysis of the capture efficacy of the axial and radial trajectories of drug carrier particles, which are injected into the microvascular system upstream of the cancerous tissue and captured in the tumor region using an externally applied magnetic field.

In chapter 6, an analysis of unsteady non-Newtonian Jeffrey blood flow and the transport of magnetic nanoparticles through an inclined porous artery with stenosis using the time fractional derivative is presented. The analytic solutions for the velocities of blood and magnetic nanoparticles are obtained using integral transforms, and the solutions are written in the form of Laplace convolutions. The analysis of the study reveals the effects of fractional parameters, Darcy number, Jeffrey fluid parameter, stenosis height, inclination angle, Hartmann number, shape parameter, and magnetic nanoparticles concentration parameter in the stenosis region.

In chapter 7, significant observations regarding the trajectory as well as the capture efficacy of drug carrier nanoparticles studied in chapters 4-6 are summarized. In addition, the future scope of the study related to the capture efficacy of drug carrier nanoparticles during magnetic drug targeting is clearly described.

2. Literature Review

An overview of the equations of motion and drug targeting during non-Newtonian fluid flow with the help of nanocarriers is presented in this chapter.

2.1. Governing Equations of fluid motion

In fluid mechanics, we consider the motion of a fluid under the influence of forces acting upon it. Since these forces produce an unsteady motion, their study is essentially one of the dynamics and must be based on Newton's second law of motion. Euler (1752) first formulated the mathematical model of fluid motion for inviscid fluids (fluids without friction or viscous force) by describing the relationship between the pressure, velocity, and density of a fluid [45]. His equation of fluid motion serves as a powerful tool in analyzing and predicting the motion of fluids, whether in the context of aerodynamics, hydrodynamics, or other branches of fluid mechanics. Euler's Equation of Motion forms the basis for understanding the fundamental principles behind the flight of airplanes, the behavior of water in rivers, blood flow and a wide range of phenomena occurring in various engineering applications. The missing fundamental part in Euler's equation is the fluid viscosity force, which is the important physical aspect of viscous fluids. The Navier-stokes equations are an extension of Euler's equations by introducing the viscous force.

The origin of Navier- stokes equations begins by Navier [46, 47] in 1822, who derived equations for homogenous incompressible fluids from a molecular point of view. Further, the continuous derivations of the Navier-Stokes equations are due to stokes (1845) [48]. In the period between Navier (in 1822) to Stokes (in 1845), the other three main scholars: Cauchy, Poisson and Saint-Venant, had made their contributions to establish the fluid motion equations under different assumptions [49]. The Navier-Stokes equations are generally treated as the universal basis of fluid mechanics, no matter how complicated and unpredictable the behavior of its solutions may be. The Navier-Stokes equations are the fundamental partial differential equations that describe the flow of fluids. Also, the motion of viscous fluid substances, such as liquids and gas with the application of Newton's second law to the fluid motion together with the assumption that the fluid stress is the sum of a diffusion viscous term (proportional to the gradient of velocity) plus pressure term.

2.1.1. Navier – Stokes equations

The Navier–Stokes equations are a nonlinear partial differential equation, which governs the motion of real viscous fluids and can be seen as Newton’s second law of motion for fluids. In the case of an incompressible Newtonian fluid, the Navier–Stokes equation in vector form is given by [50]

$$\begin{aligned}\frac{\partial u}{\partial t} + u \frac{\partial u}{\partial x} + v \frac{\partial u}{\partial y} + w \frac{\partial u}{\partial z} &= f_{Bx} - \frac{1}{\rho} \frac{\partial p}{\partial x} + \nu \left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 u}{\partial z^2} \right), \\ \frac{\partial v}{\partial t} + u \frac{\partial v}{\partial x} + v \frac{\partial v}{\partial y} + w \frac{\partial v}{\partial z} &= f_{By} - \frac{1}{\rho} \frac{\partial p}{\partial y} + \nu \left(\frac{\partial^2 v}{\partial x^2} + \frac{\partial^2 v}{\partial y^2} + \frac{\partial^2 v}{\partial z^2} \right), \\ \frac{\partial w}{\partial t} + u \frac{\partial w}{\partial x} + v \frac{\partial w}{\partial y} + w \frac{\partial w}{\partial z} &= f_{Bz} - \frac{1}{\rho} \frac{\partial p}{\partial z} + \nu \left(\frac{\partial^2 w}{\partial x^2} + \frac{\partial^2 w}{\partial y^2} + \frac{\partial^2 w}{\partial z^2} \right).\end{aligned}\tag{2.1}$$

The Navier – Stoke’s equations (Eq. 2.1) in vector notation:

$$\frac{\partial \mathbf{V}}{\partial t} + (\mathbf{V} \cdot \nabla) \mathbf{V} = \mathbf{f}_B - \frac{1}{\rho} \nabla P + \nu \nabla^2 \mathbf{V},\tag{2.2}$$

where

$$\Delta P = \left(\frac{\partial p}{\partial x}, \frac{\partial p}{\partial y}, \frac{\partial p}{\partial z} \right)^T, \nabla^2 \mathbf{V} = \frac{\partial^2 \mathbf{V}}{\partial x^2} + \frac{\partial^2 \mathbf{V}}{\partial y^2} + \frac{\partial^2 \mathbf{V}}{\partial z^2}, \mathbf{V} \cdot \nabla = u \frac{\partial}{\partial x} + v \frac{\partial}{\partial y} + w \frac{\partial}{\partial z},\tag{2.3}$$

$\mathbf{V}$ is the velocity vector, $\mathbf{f}_B$ is the body force vector, P is pressure, $\nu = \frac{\mu}{\rho}$ is the kinematic

viscosity, μ is the dynamic viscosity, and ρ is the density. If we call the left hand side of Eq.

(2.2), $\frac{\partial \mathbf{V}}{\partial t} + (\mathbf{V} \cdot \nabla) \mathbf{V} = \mathbf{a}$, the acceleration of the fluid particle, and the right hand side

$\mathbf{f}_B - \frac{1}{\rho} \nabla P + \nu \nabla^2 \mathbf{V} = \sum \mathbf{F}_{ext}$, the summation of the external forces that act on the fluid particle per

unit of mass, we have that $\sum \mathbf{F}_{ext} = \mathbf{a}$, which is Newton’s second law of motion per unit of mass.

The acceleration $\mathbf{a}$ is composed of two parts, the first part $\frac{\partial \mathbf{V}}{\partial t}$, which is the local acceleration,

and reflects the change in velocity with time observed in a fixed point in the flow as the particles

pass by. The second part $(\mathbf{V} \cdot \nabla)\mathbf{V}$ is the convective acceleration. It reflects the change in velocity of a particle in space as the particle moves from one point to another in the flow field in an infinitesimal time. Whereas f_B , represents the body force per unit of mass (such as the gravitational force or the electromagnetic force) that acts on the fluid particle. $\frac{1}{\rho}\nabla P$ is the pressure term, and indicates that the fluid flows in the direction of the largest change in pressure; $\nu \nabla^2 \mathbf{V}$ is the viscous term, and indicates the friction force due to the viscosity acting on the fluid particle as it moves with velocity $\mathbf{V}$. Both the pressure force and the viscous force are the forces that act at the surface of the fluid particle, and as such are classified as external forces

The Navier–Stokes equations are an evolution of Euler’s equation. This equation governs the motion of the perfect non viscous fluid and as such can be seen like the Navier–Stokes equation without the viscous term $\nu \nabla^2 \mathbf{V}$. Euler’s equation written in vector notation looks

$$\frac{\partial \mathbf{V}}{\partial t} + (\mathbf{V} \cdot \nabla)\mathbf{V} = f_B - \frac{1}{\rho} \nabla P + \nu \nabla^2 \mathbf{V}. \quad (2.4)$$

For an incompressible fluid, the Navier – Stokes equations in cylindrical coordinates (r, θ, z) can take the form [51]

$$\begin{aligned} \frac{Du_r}{Dt} - \frac{u_\theta}{r} &= f_r - \frac{1}{\rho} \frac{\partial p}{\partial r} + \nu \left(\nabla^2 u_r - \frac{u_r}{r^2} - \frac{2}{r^2} \frac{\partial u_\theta}{\partial \theta} \right), \\ \frac{Du_\theta}{Dt} - \frac{u_\theta u_r}{r} &= f_\theta - \frac{1}{r} \frac{1}{\rho} \frac{\partial p}{\partial \theta} + \nu \left(\nabla^2 u_\theta - \frac{u_\theta}{r^2} + \frac{2}{r^2} \frac{\partial u_r}{\partial \theta} \right), \\ \frac{Du_z}{Dt} &= f_z - \frac{1}{\rho} \frac{\partial p}{\partial z} + \nu \nabla^2 u_z, \end{aligned} \quad (2.5)$$

where, u_r , u_θ , u_z are the velocities in r , θ , z cylindrical coordinate direction, p is the pressure,

f_r , f_θ , f_z are the body force components in r , θ , z directions and the operators $\frac{D}{Dt}$ and ∇^2 are

$$\begin{aligned}\frac{D}{Dt} &= \frac{\partial}{\partial t} + u_r \frac{\partial}{\partial r} + \frac{u_\theta}{r} \frac{\partial}{\partial \theta} + u_z \frac{\partial}{\partial z}, \\ \nabla^2 &= \frac{\partial^2}{\partial r^2} + \frac{1}{r} \frac{\partial}{\partial r} + \frac{1}{r^2} \frac{\partial^2}{\partial \theta^2} + \frac{\partial^2}{\partial z^2}.\end{aligned}\tag{2.6}$$

2.2. Non-Newtonian fluids

Newtonian fluids are defined to be those fluids exhibiting a direct proportionality between shear stress and shear strain rate. In more precise technical terms, Newtonian fluids are characterized by the assumption that the extra stress tensor, which is the part of the total stress tensor that represents the shear and extensional stresses caused by the flow excluding hydrostatic pressure, is a linear isotropic function of the components of the velocity gradient, and therefore exhibits a linear relationship between stress and the rate of strain [52-54]. On the contrary, non-Newtonian fluids may reveal a nonlinear relationship between the fluid stress and an applied shear rate. Some of the most characteristic features of non-Newtonian behavior are strain dependent viscosity, time-dependent viscosity, yield-stress where a certain amount of stress should be reached before the flow starts, and stress relaxation where the resistance force on stretching fluid element will first rise sharply then decay with a characteristic relaxation time [55]. Non-Newtonian fluids are commonly divided into three broad groups, namely time-independent fluids, time-dependent fluids, and viscoelastic fluids [56, 57]. Viscoelastic fluids are those that show partial elastic recovery upon the removal of a deforming stress. Such materials possess properties of both viscous fluids and elastic solids.

The interactions between the macromolecular structures in non-Newtonian fluids are very complex in many rheological interesting systems hence, the chemical and physical properties of these liquids cannot be easily modeled. As an alternative, constitutive equations are derived based on the continuum mechanics to predict the non-Newtonian fluid behaviors. Different constitutive equations can be used to classify the systems into inelastic and elastic fluids. In the inelastic fluid models, for example, Carreau, Power-law and Bingham models, the focus is mostly on the instantaneous change of the fluid viscosity with the applied shear rate. These models are comparatively simple to be utilized in numerical and analytical investigations; however, they cannot capture all the features of the different non-Newtonian fluids such as memory and elasticity effects. In the elastic fluid models, for instance. In Maxwell and Jeffrey models, the fluid stress

does not change instantaneously with the shear rate to account for the memory effect of the flow [58]. To model viscoelastic non-Newtonian fluids, often the viscous and elastic effects are put together based on an identical principle as a mechanical system including dashpots and nonlinear elastic spring [59]. Although the non-Newtonian models are idealized, they can capture the different behaviors of various real fluids under specific conditions.

Under some critical conditions, blood behaves as a non-Newtonian fluid. Blood is a concentrated fluid of numerous cellular constituents involving white blood cells (leukocytes or WBCs), red blood cells (RBCs or erythrocytes) and platelets (thrombocytes), in an ionic solution and aqueous polymeric solution called plasma [60]. The viscosity of blood depends on the hematocrit, shear rate, protein content in plasma, temperature and vessel diameter. The non-Newtonian nature of blood is seen to have a very significant effect on flow properties at low shear rate in small arteries and capillaries [61, 62]. The rheological properties of blood are strongly influenced by the aggregation, deformation and alignment of the red cells at different shear rates. At low shear rate, the fibrinogen and globulins in plasma assist to aggregate red cells in the form of a three-dimensional microstructure which is observed in both physiological and pathological conditions. This microstructure is called rouleaux which leads to the shear thinning nature of blood. Also, the formation of 3-D microstructure may be one of the reasons for the consideration of yield stress as well as apparent viscosity of the blood.

Due to the non-Newtonian characteristic of red blood cells, in our work we represent blood rheology by the non-Newtonian time fractional Casson, Jeffrey and Maxwell fluids. For the first time (in 1958) Casson [63] basing his calculations on certain assumptions considering the magnitude of inter-particle forces and disruptive stress in chain like floccules present in varnishes and printing inks, derived the semi-empirical equation to describe their flow behavior. A year later Reiner and Blaire [64] found that Casson's description is also suitable for the flow of blood. Since then, there have been various studies supporting the use of the Casson equation in blood rheology. On the other hand, the advantage of considering Jeffrey and Maxwell fluids as blood rheology is that red blood cells behave like a viscoelastic material having the properties of elasticity and viscosity [65, 66]. Thus, our study focused on drug targeting during Casson, Jeffrey and Maxwell fluid flow in the microvessel. The constitutive equations of these three fluids are described in Table 2 -1 with the parameters: τ is the Cauchy stress tensor, S is the extra stress tensor, μ is the

dynamic viscosity, and λ_1 and λ_2 are the material parameters of the Jeffrey fluid; V is the velocity vector ; p is the pressure, I is the identity matrix, λ is the relaxation time of Maxwell fluid, the Rivlin–Ericksen tensor A_1 is defined through $\nabla V + (\nabla V)^T$. p_y is the yield stress of the fluid, μ_b is the plastic dynamic viscosity of the Casson fluid, π is the product of the component of deformation rate with itself (i.e., $\pi = e_{ij}e_{ij}$, with $e_{ij} = \frac{1}{2}(\frac{\partial v_i}{\partial x_j} + \frac{\partial v_j}{\partial x_i})$), e_{ij} is the $(i, j)^{th}$ component of the deformation rate and π_c is the critical value based on the Casson model. In case $\pi > \pi_c$ the fluid flow takes place generating the velocity field.

Table 2 - 1 Constitutive equations of Maxwell, Jeffrey and Casson fluids.

Nº	Fluids	Constitutive Equations	References
1	Maxwell	$\tau = -PI + S,$ $S + \lambda(\frac{\partial S}{\partial t} + V \cdot \nabla S - LS - SL^T) = \mu A_1, L = \nabla V$	[67]
2	Jeffrey	$\tau = -PI + S,$ $S = \frac{\mu}{1 + \lambda_1} [A_1 + \lambda_2(\frac{\partial A_1}{\partial t} + V \cdot \nabla)A_1],$	[68]
3	Casson	$\tau_{ij} = \begin{cases} 2(\mu_b + \frac{p_y}{\sqrt{2\pi}})e_{ij}, \pi > \pi_c, \\ 2(\mu_b + \frac{p_y}{\sqrt{2\pi_c}})e_{ij}, \pi < \pi_c, \end{cases}$	[69]

2.3 Solution Approach

Navier – Stokes equations of blood flow are partial differential equations that govern the motion of blood in the blood vessel. Several solution approaches, numerical and analytic methods, have been developed to solve such problems based on different conditions such as unidimensional or multidimensional flows, multiphase flows, geometries of the flow region (for example, branching vessel and stenosed vessel), and so on.

Numerical methods such as the finite difference method, finite element method, and finite volume method are the methods used to find approximate solutions to a problem rather than the exact ones. Numerical simulation techniques such as the finite element method, finite volume method, and computational fluid dynamics have proven to be valuable tools that enabled researchers to model complex geometries, accurately simulate blood flow parameters [70], model multiphase flows, and model multidimensional flows [71]. Numerical methods have great importance and wide application in engineering and have played a very significant role in the development of technical sciences. They are used to solve complex problems in higher mathematics with the help of computers. The main advantage of numerical methods is that the solution can be obtained even in cases where it is not possible to obtain an analytical solution. However, numerical methods provide solutions that are always approximated but mostly accurate enough from the aspect of engineering accuracy. In addition, they require higher computational time as compared to analytic approaches [72].

Analytical methods should be used if the blood flow equation can be simplified to a one-dimensional problem. The main advantages of analytical methods are the good transparency between calculated results and data input, less effort in modeling and programming, and very short computation time. However, they require a strong mathematical background and are limited to relatively simple problems compared to numerical methods [73]. Solving a one-dimensional problem analytically involves finding exact solutions using various mathematical methods. In this thesis, we applied the semi-analytic approach to solve the one-dimensional governing time fractional mathematical models of blood flow with magnetic nanoparticles in the microvessel. We used the Laplace, and finite Hankel transforms along with their inverse with the help of special functions to find the velocity of blood and magnetic nanoparticles. The Laplace transform is very important to apply when the fluid model is defined in the time domain, while the Hankel transform is used to solve problems involving axisymmetric flow. The trajectories of drug carrier magnetic nanoparticles in the radial and axial directions are obtained numerically using the fourth-order Runge-Kutta (RK-4) method.

3. Mathematical Preliminaries

In this chapter, we present some basic concepts and definitions related to this thesis.

3.1. Basic definitions

3.1.1. The Gamma function:

The Gamma function is most important when defining a Bessel function.

Definition 1: Let z be a complex number with $\Re(z) > 0$. The Gamma function denoted by Γ is defined by [74]

$$\Gamma(z) = \int_0^{\infty} e^{-t} t^{z-1} dt. \quad (3.1)$$

Integrating by parts, we get the following recurrence relation

$$\Gamma(z+1) = z\Gamma(z). \quad (3.2)$$

The Gamma function is the generalization of the factorial to complex numbers. In fact, for all $n \in \mathbb{N} \cup \{0\}$,

$$\Gamma(n+1) = n! \quad (3.3)$$

3.1.2. Special functions

Definition 2: Robotnove – Hartley [75]

$$F_{\alpha}(-\chi, t) = \sum_{m=0}^{\infty} \frac{(-\chi)^m t^{(m+1)\alpha-1}}{\Gamma[(m+1)\alpha]}, \quad \alpha > 0, \quad (3.4)$$

Definition 3: Lorenzo – Hartely [76]

$$R_{\alpha, \nu}(-\chi, t) = \sum_{m=0}^{\infty} \frac{(-\chi)^m t^{(m+1)\alpha-1-\nu}}{\Gamma[(m+1)\alpha-\nu]}, \quad \text{Re}(\alpha-\nu) > 0, \quad (3.5)$$

3.2. Integral transforms

Mathematical operators known as integral transforms produce a new function $g(y)$ by integrating the product of an existing function $f(x)$ and an integral kernel function $K(x, y)$ between suitable limits. The solution can then be mapped back to the original domain with the inverse of the integral transform. The importance of integral transforms is mainly in solving differential equations, fractional derivatives, algebraic equations, signal and image processing, spectral analysis of stochastic processes [77 – 79].

3.2.1. Laplace transform

Definition 4: Let s be a complex number with $\text{Re}(s) > 0$. The Laplace transform of $f(t)$ is defined by [80]

$$L[f(t)] = \int_0^{\infty} e^{-st} f(t) dt = F(s). \quad (3.6)$$

The Laplace transform is a mapping from points in the t domain to points in the s domain.

3.2.1.1 Some important properties of Laplace transform

The Laplace transform has many interesting and useful properties, the most fundamental of which is linearity. For instance, the linearity property is the property that enables us to add results together to deduce other more complicated ones.

3.2.1.2. Linearity property:

Let A and B be any constants and $f(t)$ and $g(t)$ be functions whose Laplace transform exists, then [80]

$$L[Af(t) + Bg(t)] = AL[f(t)] + BL[g(t)]. \quad (3.7)$$

3.2.1.3. Derivative of order n :

Suppose a differentiable function $f(t)$ has Laplace transform $F(s)$, then the Laplace transform of the n^{th} derivative of $f(t)$ is given by [81]

$$\begin{aligned} L\left[\frac{d^n}{dt^n} f(t)\right] &= s^n F(s) - s^{(n-1)} f(0) - s^{(n-2)} f'(0) - \dots - f^{(n-1)}(0) \\ &= s^n F(s) - \sum_{k=1}^n s^{n-k} f^{(k-1)}(0). \end{aligned} \quad (3.8)$$

3.2.1.4. Convolution property:

The convolution of two given functions $f(t)$ and $g(t)$ is written $f(t) * g(t)$ and defined by [81]

$$f(t) * g(t) = \int_0^t f(\tau) g(t - \tau) d\tau. \quad (3.9)$$

Remark: The Laplace transform of the convolution of two functions is the product of their Laplace transforms. That is,

$$L[f(t) * g(t)] = L\left[\int_0^t f(\tau) g(t - \tau) d\tau\right] = L[f(t)] L[g(t)]. \quad (3.10)$$

3.2.1.5. Integral Property [81]:

If $L[f(t)] = F(s)$, then

$$L\left[\int_0^t f(t) dt\right] = \frac{F(s)}{s}. \quad (3.11)$$

Definition 5: Inverse Laplace transform:

If $f(t)$ has the Laplace transform $F(s)$, that is $L[f(t)] = F(s)$, then the inverse Laplace transform is defined by [81]

$$L^{-1}[F(s)] = f(t), \quad (3.12)$$

and is unique apart from null functions.

Remark: The inverse Laplace transformation is linear, i.e.,

$$L^{-1}[af(t) + bg(t)] = aL^{-1}[f(t)] + bL^{-1}[g(t)] \quad (3.13).$$

3.2.2. Hankel Transform

The Hankel transform involving Bessel functions as the kernel arises naturally in axisymmetric problems formulated in cylindrical polar coordinates. The use of the joint Laplace and Hankel transforms is very important in solving several partial differential equation models.

Definition 6: Let $f(r)$ be a function defined for $r \geq 0$. The n^{th} order Hankel transform of $f(r)$ is defined as [82]

$$F_n(r) = H_n\{f(r)\} = \int_0^\infty r f(r) J_n(sr) dr, \quad (3.14)$$

where, $J_n(\cdot)$ is the n^{th} order Bessel function.

If $n > -\frac{1}{2}$, Hankel's repeated integral immediately gives the inversion formula

$$f(r) = H_n^{-1}\{F_n(s)\} = \int_0^\infty s F_n(s) J_n(sr) ds. \quad (3.15)$$

In particular, the Hankel transforms of the zero order ($n = 0$) and of order one ($n = 1$) are often useful for the solution of problems involving Laplace's equation in an axisymmetric cylindrical geometry.

3.2.3. Finite Hankel Transform

Definition 7: The finite Hankel transform of order n of a function $f(r)$ is denoted by [83]

$H_n\{f(r)\} = \tilde{f}_n(k_i)$ and is defined by

$$H_n\{f(r)\} = \tilde{f}_n(k_i) = \int_0^a r f(r) J_n(r k_i) dr. \quad (3.16)$$

The inverse finite Hankel transform is then defined by

$$H_n^{-1}\{\tilde{f}_n(k_i)\} = f(r) = \frac{2}{a^2} \sum_{i=1}^{\infty} \tilde{f}_n(k_i) \frac{J_n(r k_i)}{J_{n+1}^2(a k_i)}, \quad (3.17)$$

where the summation is taken over all positive roots of $J_n(a k_i) = 0$. The zero-order finite Hankel transform, and its inverse are defined by

$$H_0\{f(r)\} = \tilde{f}_0(k_i) = \int_0^a r f(r) J_0(r k_i) dr, \quad (3.18)$$

$$H_0^{-1}\{\tilde{f}_0(k_i)\} = f(r) = \frac{2}{a^2} \sum_{i=1}^{\infty} \tilde{f}_0(k_i) \frac{J_0(r k_i)}{J_1^2(a k_i)}, \quad (3.19)$$

where the summation is taken over the positive roots of $J_n(a k_i) = 0$.

Similarly, the first-order finite Hankel transform, and its inverse are

$$H_1\{f(r)\} = \tilde{f}_1(k_i) = \int_0^a r f(r) J_1(r k_i) dr, \quad (3.20)$$

$$H_1^{-1}\{\tilde{f}_1(k_i)\} = f(r) = \frac{2}{a^2} \sum_{i=1}^{\infty} \tilde{f}_1(k_i) \frac{J_1(r k_i)}{J_2^2(a k_i)}, \quad (3.21)$$

where k_i is chosen as a positive root of $J_n(a k_i) = 0$.

3.3. Fractional Calculus

Fractional calculus is a name for the theory of integrals and derivatives of arbitrary order, which unifies and generalizes the notions of integer-order differentiation and n -fold integration. Fractional calculus is three centuries old as conventional calculus, but not very popular amongst the science and engineering community. The beauty of this subject is that fractional derivatives (and integrals) are not a local (or point) property (or quantity). This considers the history and non-local distributed effects. In other words, perhaps this subject translates the reality of nature better [80]. Following Leibniz's and L'Hopital's first inquisition, the study of fractional calculus was primarily reserved for the best minds in mathematics. As it is known, several physical phenomena

are described by fractional derivatives [84]. This is due to the known fact that fractional operators take into account the system evolution, by considering both the global and local characteristics. In addition, experimental results are sometimes contradicted by integer-order calculus and therefore non-integer-order derivatives may be more suitable [85].

Several great mathematicians that dabbled with fractional calculus and who have provided significant contributions up to the middle of our century are found in [86 – 91] and the references therein. Afterwards, fractional calculus has become an attractive subject to engineers, mathematicians and physicists, and various forms of non-integer differential operators such as the Grünwald–Letnikov, Hadamard, Riemann–Liouville, Caputo, Hilfer [92], Kilbas et al. [93], Podlubny [94], Samko et al. [95], Cresson [96], and so on. Agrawal [97] introduced an interesting perspective to the subject by unifying all previously mentioned notions of fractional derivatives and integrals and later studied in Bourdin et al. [98].

Many found, using their own notation and methodology, definitions that are well fitted to the concept of an arbitrary (non-integer) order derivative or integral. The most famous definitions that have been widely popularized in the world of fractional calculus are the Riemann–Liouville, Grünwald–Letnikov, Caputo and recently Caputo – Fabrizio and Atangana – Baleanu definitions. In our thesis, we have only used Caputo and Caputo – Fabrizio definitions of fractional derivatives, which are briefly explained in the following section.

3.3.1. Fractional derivatives

3.3.1.1. Caputo Fractional Derivative

Caputo fractional derivative is seen as a good alternative method to the Riemann–Liouville type for computing fractional derivative. It was first introduced in the research work [99] by M. Caputo and two years later in his book [100].

Definition 8: The Caputo fractional derivative of order α^{th} for a function $f(t)$ can be written as [80]

$${}_a^C D_t^\alpha f(t) = \frac{1}{\Gamma(q-\alpha)} \int_a^t \frac{f^{(q)}(\tau)}{(t-\tau)^{\alpha-1+q}} d\tau, \quad (q-1 < \alpha < q). \quad (3.22)$$

Under natural and normal conditions on $f(t)$ when $a = 0$, the Caputo fractional derivative of α^{th} order can be simplified as ${}^C D_t^\alpha f(t)$.

For $(0 < \alpha < 1)$ and $a = 0$, the Caputo derivative reduces to

$${}^C D_t^\alpha f(t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t \frac{f'(\tau)}{(t-\tau)^\alpha} d\tau, \quad (0 < \alpha < 1). \quad (3.23)$$

Fractional calculus, and particularly Caputo fractional derivative, find numerous applications in different areas of science [92, 99, 101, 102]

3.3.1.2. Caputo – Fabrizio Fractional derivative

Definition 9:

Let $0 < \alpha < 1$. The fractional Caputo-Fabrizio derivative of order α^{th} of a function $f(t)$ is given by [103]

$${}^{C-F} D_t^\alpha f(t) = \frac{1}{1-\alpha} \int_0^t \exp\left(-\frac{\alpha(t-\tau)}{1-\alpha}\right) f'(\tau) d\tau, \quad t \geq 0. \quad (3.24)$$

4. Contribution of rational design and fractional rheology on magnetic nanoparticle-based drug targeting in a microvessel with Saffman force*

4.1. Introduction

In the applications of nanotechnology, the delivery of drugs using nanoparticles plays an important role in medical science and bioengineering fields. Some applications of nanoparticles include gene delivery, medical, optical, and magnetic resonance imaging [104 – 108]. Drug targeting is a means of providing drugs to an infected organ in such a way that the accumulation of drugs takes place in the target region of the tissue at the cellular or sub-cellular level. Recent studies show that magnetic nanoparticle-based drug targeting (MNBDT) in the occurrence of a magnetic field is an imperative and promising medication technique, where the transportation of drugs to an affected area is guided by magnetic field. MNBDT is a promising drug delivery method because of its high potential efficacy, harmless nature, and economic importance [109]. This kind of medication is aimed at targeting localized diseases in particular areas, like cancerous tumor cells. It can be efficiently achieved if magnetic nanoparticles possess strong magnetic moments that can be influenced by a magnetic field [110]. In this kind of medication, the magnetic field produced by an external magnet guides the trajectories of drug-carrier magnetic nanoparticles (DCMNPs) to the cancerous tumor region. In addition to the magnetic field that significantly affects the trajectories of drug-carrier magnetic nanoparticles, there are also certain factors that affect the efficacy of the trajectories of drug-carrier magnetic nanoparticles during MNBDT. Such factors include the rheology of the blood, the shape and size of drug-carrier magnetic nanoparticles, the permeability of the blood vessel wall, the uplift force, and others. The shape of drug-carrier magnetic nanoparticles performs a significant function in drug loading and release, biocompatibility, circulation time, targeting, and subcellular adoption. In recent developments, different shapes of drug carrier particles have been developed. Because of their symmetric nature and the presence of well-defined models of hydrodynamic interactions [27], and thermodynamic

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favorability [111] spherical drug-carrier magnetic nanoparticles are widely used in drug delivery. Subject on the size and shape of the cells or organs, non-spherical drug-carrier magnetic nanoparticles, such as ellipsoids, cylinders, cones, discs, and biconcave discoids [29 - 31], ellipsoidal (oblate, and prolate) [32], are applicable in various areas of the organs. However, the use of non-spherical drug-carrier magnetic nanoparticles for drug delivery is limited due to a lack of techniques to fabricate non-spherical biocompatible drug-carrier magnetic nanoparticles [112]. In spite of the inadequate availability of non-spherical drug-carrier magnetic nanoparticles, carrier shape has a significant effect on cellular internalization, margination towards the target region, and trajectories towards the tumor region [113 – 117].

Unlike classical calculus, which is widely applicable in dynamical systems, the relevance of fractional calculus has recently captured the interest of researchers in various fields. Due to their memory effect, fractional derivatives contain more information about the past behavior of the physical system. The memory effect of fractional derivatives fascinated researchers, who conducted investigations in various areas of interest [118 –122]. Among the fractional derivatives models, the most used fractional models are Caputo and Caputo-Fabrizio (C-F) fraction models. For example, Shah et al. [123] studied a mathematical model by trading the classical first-order time derivative with a Caputo time fractional derivative to examine the flow properties of fluid through an axisymmetric vessel. In their work, they found analytic solutions for blood and magnetic nanoparticles velocities. Ali et al. [124] devoted the Caputo time-fractional model to examine the impact of magnetic field on Casson blood flow through a microvessel. Jamil et al. [125] analyzed the non-Newtonian blood flow through a stenotic artery in the presence of magnetic field and an oscillating pressure gradient by applying the C-F time fractional model. Excellent applications on fluid flow using fractional models are also found in refs. [126 – 131]. Viscoelastic fluids are fluids that obey non-Newtonian fluid properties and exhibit both viscous and elastic properties. Some examples of viscoelastic fluids include biological fluids, suspensions of Deoxyribonucleic Acid (DNA), polymers, and others. These fluids are widely applicable in industry and biomedical engineering fields. Maxwell fluid is a viscoelastic fluid that is widely used and has gained the interest of various researchers. Bai et al. [132] examined the heat transfer and viscous dissipation effects of fractionalized magnetohydrodynamics (MHD) Maxwell fluids by applying the finite difference numerical technique. Zhang et al. [133] examined the hemodynamic nature of the fractional Maxwell fluid flow through the stenotic artery. Tang et al. [134] conducted

a comparative study on the natural convective transport of fractional Maxwell fluid by using Caputo and C-F time fractional models. Kot and Elmaboud [135] studied the heat transfer characteristics of unsteady fractional Maxwell fluid flow across a vertical artery with stenosis. Biomagnetic fluid dynamics is an important area of research related to biological fluid flow under the impact of magnetic field. These fluids have various functions in the fields of medical science and bioengineering. Some applications include the selective carriage of drugs using magnetic nanoparticles as drug carriers, magnetic hyperthermia to treat cancer cells, and the development of magnetic tracers. Magnetohydrodynamics is the study of electrically conducting fluid in the magnetic field, which plays an essential role in industrial and engineering applications [136]. Rehman et al. [137] employed Prabhakar fractional derivatives to analyze the influences of thermal and concentration on magnetohydrodynamics Maxwell fluid flow with variable velocity. Aman et al. [138] conferred the impacts of second-order slip on fractionalized magnetohydrodynamics Maxwell fluid flow in the incidence of a moving plate. Liu et al. [139] demonstrated fractional magnetohydrodynamics Maxwell fluid in a square cavity influenced by Hall effects and radiation. Other findings on fractional Maxwell blood flow are found in refs. [140 – 142]. As per authors' knowledge, no one has considered the transport of drug-carrier magnetic nanoparticles with various shapes through the microvessel to the cancerous tumor cells during magnetic drug targeting by assuming the rheology of blood with non-Newtonian Maxwell fluid feature theoretically in a Caputo-Fabrizio fractional sense.

From the above literature, very few researchers work on the blood flow with aspect of the fractional derivative and among them no-one has considered the trajectories of the drugs carrying magnetic nanoparticles during the magnetic drug targeting by treating blood as Maxwell fluid. As a result, the present study is aimed to fill this gap. The novelty of the present problem involves:

- (a) Analyze the trajectories of the drugs carrying magnetic nanoparticles (DCMNPs) during the magnetic drug targeting is considered.
- (b) Analyze the impact of the memory effect by considering the blood flow equation represented with C-F fractional time derivative differential equations is incorporated.
- (c) The viscoelastic Maxwell fluid represents the rheology of blood.
- (d) The study considered the impact of the shape of drug carriers, Saffman force, and blood-particle interactions in the governing system.

Firstly, an analytic expression is written for the velocity of fluid using Laplace transform (LT) and finite Hankel transform (FHT) of order zero with corresponding inverses, and then we write the analytic approach for the average blood velocity as functions of Laplace convolutions and a Bessel function of the first order and first kind. Secondly, we compute the trajectories of drug-carrier magnetic nanoparticles and the total volume fraction (VF) of magnetic nanoparticles numerically and displayed in graphical form. The present work will help biomedical engineers and nanomedicine researchers develop magnetic devices and the next generation of drug carriers to treat localized diseases like cancerous tumors.

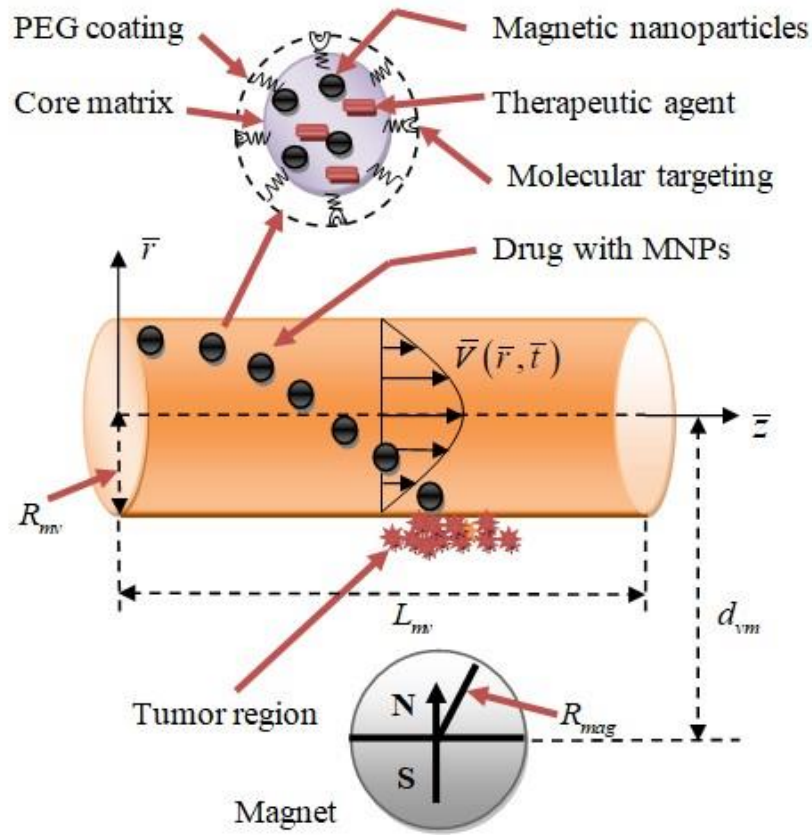


Figure 4.1 Non-invasive trajectories of drug-carrier magnetic nanoparticles with reference frame.

4.2. Mathematical formulations

We consider unsteady, and incompressible, fully developed Maxwell fluid flow of blood (fluid properties independent of temperature) in a permeable horizontal cylindrical artery of radius R_{mv}

and length L_{mv} , and polar coordinates $(\bar{r}, \bar{\theta}, \bar{z})$ representing the radial $(\bar{r})$, circumference $(\bar{\theta})$, and the axial flow $(\bar{z})$ directions, respectively (see Fig. 4-1). We assume that the magnetic nanoparticles are uniformly distributed throughout the blood vessel. A uniform magnetic field acts in a normal direction towards the flow of motion. The flow is irrotational and axisymmetric along the $\bar{z}$ -axis of the artery with a function of r only. The resulting momentum equation governing the flow as derived using afore mentioned assumptions is [133, 143]

$$\frac{\partial \bar{V}}{\partial \bar{t}} = -\frac{1}{\rho} \frac{\partial \bar{p}}{\partial \bar{z}} + \frac{1}{\rho \bar{r}} \frac{\partial}{\partial \bar{r}} (\bar{r} \bar{T}_{\bar{r}\bar{z}}) - \frac{\nu}{k_p} \bar{V} - \frac{\sigma B_0^2}{\rho} \bar{V}. \quad (4.1)$$

The Maxwell constitutive equation is given by [137]

$$\left(1 + \bar{\lambda} \frac{\partial}{\partial \bar{t}}\right) \bar{T}_{\bar{r}\bar{z}} = \mu \frac{\partial \bar{V}}{\partial \bar{r}}, \quad (4.2)$$

where $\bar{T}_{\bar{r}\bar{z}}$ is the Maxwell tangential stress and μ is the dynamic viscosity of fluid.

Upon substitution of Eq. (4.2) into Eq. (4.1) leads to

$$\begin{aligned} \left(1 + \bar{\lambda} \frac{\partial}{\partial \bar{t}}\right) \frac{\partial \bar{V}}{\partial \bar{t}} = & \left(1 + \bar{\lambda} \frac{\partial}{\partial \bar{t}}\right) \frac{1}{\rho} \left(-\frac{\partial \bar{p}}{\partial \bar{z}}\right) + \nu \left(\frac{\partial^2 \bar{V}}{\partial \bar{r}^2} + \frac{1}{\bar{r}} \frac{\partial \bar{V}}{\partial \bar{r}}\right) - \left(1 + \bar{\lambda} \frac{\partial}{\partial \bar{t}}\right) \frac{\nu}{k_p} \bar{V} \\ & - \left(1 + \bar{\lambda} \frac{\partial}{\partial \bar{t}}\right) \frac{\sigma B_0^2}{\rho} \bar{V}, \end{aligned} \quad (4.3)$$

where, $\rho, -\frac{\partial \bar{p}}{\partial \bar{z}}, \bar{\lambda}, \nu, k_p, \sigma, B_0$ and $\bar{V}$ are the density of fluid, the oscillating pressure gradient, the

Maxwell parameter (relaxation time parameter), the kinematic viscosity, the permeability, the electrical conductivity, the applied magnetic field, and the axial velocity of the fluid, respectively.

The proper initial and boundary values relating to Eq. (4.3) can be written as

$$\bar{V}(\bar{r}, 0) = \frac{\partial \bar{V}(\bar{r}, 0)}{\partial \bar{t}} = 0 \text{ for } \bar{t} = 0, \bar{r} \in [0, R_{mv}], \bar{V}(R_{mv}, \bar{t}) = 0, \frac{\partial \bar{V}(0, \bar{t})}{\partial \bar{r}} = 0, \bar{t} > 0. \quad (4.4)$$

We introduce the following non-dimensional parameters for the purpose of dimensionless study [137]

$$r = \frac{\bar{r}}{R_{mv}}, t = \frac{\nu_{cp} \bar{t}}{R_{mv}}, V = \frac{\bar{V}}{\nu_{cp}}, \lambda = \frac{\nu_{cp} \bar{\lambda}}{R_{mv}}, p = \frac{\bar{p}}{\rho \nu_{cp}^2}, z = \frac{\bar{z}}{R_{mv}}, \quad (4.5)$$

where, ν_{cp} is the velocity of drug-carrier magnetic nanoparticles.

Using Eq. (4.5) into Eqs. (4.3) and (4.4) yields the dimensionless momentum equation

$$\begin{aligned} \frac{\partial V}{\partial t} + \lambda \frac{\partial}{\partial t} \left(\frac{\partial V}{\partial t} \right) = & \left(1 + \lambda \frac{\partial}{\partial t} \right) \left(-\frac{\partial p}{\partial z} \right) + \frac{1}{\text{Re}} \left(\frac{\partial^2 V}{\partial r^2} + \frac{1}{r} \frac{\partial V}{\partial r} \right) - \left(1 + \lambda \frac{\partial}{\partial t} \right) \frac{1}{\text{Da Re}} V \\ & - \left(1 + \lambda \frac{\partial}{\partial t} \right) \frac{\text{Ha}^2}{\text{Re}} V, \end{aligned} \quad (4.6)$$

with

$$V(r, 0) = \frac{\partial V(r, 0)}{\partial t} = 0 \text{ for } t = 0, \quad r \in [0, 1], \quad V(1, t) = 0, \quad \left. \frac{\partial V}{\partial r} \right|_{r=0} = 0, \quad t > 0, \quad (4.7)$$

where, $\text{Re} = \frac{R_{mv} v_{cp}}{\nu}$, $\text{Da} = \frac{k_p}{R_{mv}^2}$ are Reynolds and Darcy numbers, respectively, and

$\text{Ha} = B_0 R_{cp} \sqrt{\frac{\sigma}{\rho \nu}}$ is the magnetic parameter.

The pressure gradient of blood flow in Eq. (4.6) has the form [124, 144]

$$-\frac{\partial p}{\partial z} = h_0 + h_1 \cos(\omega t), \quad h_0 > 0, \quad (4.8)$$

where h_0 , h_1 , and ω are the steady amplitude, amplitude of the transient part, and frequency of pulsation, respectively.

Substituting Eq. (4.8) into Eq. (4.6) yields

$$\begin{aligned} \frac{\partial V}{\partial t} + \lambda \frac{\partial}{\partial t} \left(\frac{\partial V}{\partial t} \right) = & h_0 + h_1 \cos(\omega t) - \omega h_1 \lambda \sin(\omega t) + \frac{1}{\text{Re}} \left(\frac{\partial^2 V}{\partial r^2} + \frac{1}{r} \frac{\partial V}{\partial r} \right) - \left(1 + \lambda \frac{\partial}{\partial t} \right) \frac{1}{\text{Da Re}} V \\ & - \left(1 + \lambda \frac{\partial}{\partial t} \right) \frac{\text{Ha}^2}{\text{Re}} V. \end{aligned} \quad (4.9)$$

Combining the last two terms of Eq. (4.9) and relocating the equation yields

$$\frac{\partial V}{\partial t} + \lambda \frac{\partial}{\partial t} \left(\frac{\partial V}{\partial t} \right) + d_{2n} \left(1 + \lambda \frac{\partial}{\partial t} \right) V - \frac{1}{\text{Re}} \left(\frac{\partial^2 V}{\partial r^2} + \frac{1}{r} \frac{\partial V}{\partial r} \right) = h_0 + h_1 \cos(\omega t) - d_{1n} \sin(\omega t). \quad (4.10)$$

4.3. C-F fractional derivative

We employ the C-F time fractional model derived from the ordinary differential equation. The C-F is chosen for this study due to its efficacy in describing heterogeneous systems with memory effects at different spatial scales, as well as the fact that the initial conditions in C-F take the same

form as those of ordinary differential equations [145, 146]. The C-F time-fractional derivative model is given by [103]

$${}^{CF}D_t^\alpha V(r, t) = \frac{1}{1-\alpha} \int_0^t e^{\left(\frac{-\alpha(t-\tau)}{1-\alpha}\right)} \frac{\partial V(r, \tau)}{\partial \tau} d\tau, \quad 0 < \alpha < 1, \quad (4.11)$$

where the Laplace transform of Eq. (11) can be given by

$$L[{}^{CF}D_t^\alpha V(r, t)] = \frac{sL[V(r, t)] - V(r, 0)}{(1-s)\alpha + s}, \quad (4.12)$$

and

$$L[{}^{CF}D_t^{\alpha+1} V(r, t)] = \frac{s^2 L[V(r, t)] - sV(r, 0) - \frac{\partial V(r, 0)}{\partial t}}{(1-s)\alpha + s}. \quad (4.13)$$

For the purpose of time FD study, the C-F time FD is introduced into Eq. (4.10) yielding

$$\begin{aligned} D_t^\alpha V + \lambda D_t^{\alpha+1} V + d_{2n} (1 + \lambda D_t^\alpha) V - \frac{1}{\text{Re}} \left(\frac{\partial^2 V}{\partial r^2} + \frac{1}{r} \frac{\partial V}{\partial r} \right) \\ = h_0 + h_1 \cos(\omega t) - d_{1n} \sin(\omega t), \quad 0 < \alpha < 1. \end{aligned} \quad (4.14)$$

4.4. Equation of motion

During magnetic drug targeting the transport of magnetic nanoparticles is affected by some of the major forces such as magnetic force F_m , viscous drag force (fluidic force) F_f , particle/blood-cell interaction and Saffman force. Having these points in mind, Newton's 2nd law of motion governs the motion of drug-carrier magnetic nanoparticles in equilibrium [27]

$$F_m + F_f + F_s = m_{cp} \frac{dv_{cp}}{dt}, \quad (4.15)$$

where m_{cp} is the mass of the drug-carrier magnetic nanoparticles. The product on the right-hand side of Eq. (4.15) is very modest and hence negligible, because the mass of the drug-carrier magnetic nanoparticles is too small. Then the force balance yields

$$F_m + F_f + F_s = 0. \quad (4.16)$$

4.5. Particle-particle interaction

Various factors affect the cell-depleted layer width of the blood vessel. Some of these factors are vessel diameter, hematocrit, and red blood cell (RBC) deformability. The presence of a cell-depleted layer in the microvessel wall considerably reduces the apparent viscosity of blood [147]. Pries et al. [148, 149] from their experimental investigation, they developed a mathematical model of the apparent viscosity in terms of hematocrit and the diameter of the vessel, which is given by

$$\mu_{bf} = \mu_{\text{plasma}} \left[1 + (\mu_{0.45} - 1) \frac{(1 - H_D)^C - 1}{(1 - 0.45)^C - 1} \left(\frac{D_v}{D_v - 1.1} \right)^2 \right] \left(\frac{D_v}{D_v - 1.1} \right)^2, \quad (4.17)$$

where μ_{plasma} and H_D are respectively the blood plasma viscosity (in the absence of blood cells and platelets) and hematocrit.

The relative apparent viscosity about hematocrit 0.45 ($\mu_{0.45}$) and constant C are

$$\mu_{0.45} = 3.2 + 6 \exp(-0.085 D_v) - 2.44 \exp(-0.06 D_v^{0.645}), \quad (4.18)$$

$$C = (0.8 + \exp(-0.075 D_v)) \left(\frac{1}{1 + 10^{-11} D_v^{12}} - 1 \right) + \frac{1}{1 + 10^{-11} D_v^{12}}, \quad (4.19)$$

with diameter of the blood vessel D_v in micron.

During the homogeneous suspension of nanoparticles in a shear flow, the effective viscosity of the particles is affected by different factors such as volume fraction, size, nature of the nanoparticles, and others [150 - 152]. This has been mainly recognized to the complex nature of interparticle interaction conditions, which leads to mounds of different sizes and particulate masses [152]. According to the findings of Brinkman [151] and Einstein [152] the efficient viscosity of the nanofluid is significantly correlated with the viscosity of the base fluid and the volume fraction of the nanoparticles. Further, experimental works by Pasol and Feuillebois [153] suggests the following empirical formula for the viscosity of nanofluid, which also depends on the diameter of the vessel

$$\mu_{nf} = \mu_{bf} \left[1 - 2.5 \left(3.4606 \frac{D_p}{D_v} - 8.6065 \left(\frac{D_p}{D_v} \right)^2 - 1 \right) \varphi \right]. \quad (4.20)$$

where D_p , D_v and ϕ are the diameter of suspended particles, the inner diameter of the tube, and the particles volume fraction, respectively. In the present study, we consider iron oxide (Fe_3O_4) nanoparticles and blood, in which blood is used as the base fluid.

4.6. Saffman force

For small drug-carrier magnetic nanoparticles in the shear field during magnetic drug targeting, the effect of the uplift force significantly influences the particle's motion. This vertical uplift force appears on the particles perpendicular to the stream direction. This force is commonly called the Saffman lift force, and it can be written as [151, 154]

$$F_s = -k\rho R_{cp}^2 \sqrt{\nu \dot{\gamma}} (v_{cp} - V_{avg}), \quad (4.21)$$

where the constant $k = 81.2$ and $\dot{\gamma}$ is the fluid shear rate.

4.7. Fluidic force

The fluid in motion experiences a drag force, which is commonly known as fluidic force. The fluid force depends on the fluid rheology and shape of the drug-carrier magnetic nanoparticles. For drug-carrier magnetic nanoparticles experiencing fluidic force, the drag coefficient with Maxwell fluid rheology and shape factor is given by $C_D = 24k'/\text{Re}$, where k' is the shape factor and $\text{Re} = \frac{R_{mv} v_{cp}}{\nu}$ is the Reynolds number. The shape factor k' for different shapes of the drug-carrier magnetic nanoparticles is expressed by [155]

$$k' = \begin{cases} 1 & ; \text{ Sphere,} \\ \frac{8\pi}{3} & ; \text{ Circular disk,} \\ \frac{2\chi}{3} \frac{1}{\ln \chi + 0.193} & ; \text{ Cylinder, } \chi = 1.0, 1.6, 2, 2.2, \\ \frac{\sqrt{\gamma^2 - 1}}{\gamma^{1/3} \ln(\gamma + \sqrt{\gamma^2 - 1})} & ; \text{ Prolate ellipsoid, } \gamma = 1.2, 1.4, 1.6, 1.8. \end{cases} \quad (4.22)$$

with aspect ratio of ellipsoid γ (major axis with respect to minor), and aspect ratio of cylinder χ (length with respect to radius). The fluidic force on the drug-carrier magnetic nanoparticles can be expressed as

$$F_f = -\frac{1}{2} \rho A_{cp} v_{cp}^2 C_D, \quad (4.23)$$

And in simplified form

$$F_f = -12 \mu_{nf} A_{cp} k' v_{cp} / R_{mv}. \quad (4.24)$$

with cross sectional area of drug-carrier magnetic nanoparticles A_{cp} .

Decomposing Eq. (4.24) in to r and z components yield

$$F_{f_r} = -12 \mu_{nf} A_{cp} k' v_{cp,r} / R_{mv}, \quad (4.25)$$

$$F_{f_z} = -12 \mu_{nf} A_{cp} k' (v_{cp,z} - V_{avg}) / R_{mv}. \quad (4.26)$$

4.8. Magnetic force on the drug carrier particles

In noninvasive magnetic drug targeting, the magnetic nanoparticles used for applications are biocompatible metallic oxides such as Fe_3O_4 , in which the susceptibility of the material is much more than that of the blood [156]. It is worth mentioning that the magnetic nanoparticles within the drug carrier are in spherical shape and magnetic field is unaltered with fluid rheology. Further, it is understood that the diameter of the blood vessel is much shorter than the distance d_{vm} from the axis of the vessel to the center of the magnet ($R_{mv} \ll d_{vm}$, Fig. 4-1). The magnet is placed close to the tumor region and the coordinate of the magnet point is axially at the center of the tumor and radially at the distance d_{vm} from the center of the axis of the microvessel i.e., $(d_{vm}, 0)$. Using the assumptions made above and results from the work of [156] the decomposition of the magnetic force yields

$$F_{m_r}(r, z) = 1.5 \mu_0 N_{mp} W_{mp} M_s^2 R_{mag}^4 \frac{d_{vm}}{(d_{vm}^2 + z^2)^3}, \quad (4.27)$$

$$F_{m_z}(r, z) = 1.5 \mu_0 N_{mp} W_{mp} M_s^2 R_{mag}^4 \frac{z}{(d_{vm}^2 + z^2)^3}, \quad (4.28)$$

where N_{mp} is the amount of non-interacting magnetic nanoparticles with the same volume W_{mp} and embedded to the drug-carrier magnetic nanoparticles. μ_0 , M_s , R_{mag} , and z are air

permeability, magnetization parameter, radius of the magnet, and distance of the particle at the z -axis, respectively.

4.9. Solution method

4.9.1. Velocity of fluid

The analytic solution of the time fractional derivative Eq. (4.14) subject to the initial condition and boundary conditions Eq. (4.7) is presented. Applying Laplace transform to Eq. (4.14), and upon substituting the IC from Eq. (4.7) yields

$$\begin{aligned} & \frac{s}{\alpha + (1-\alpha)s} V(r, s) + \frac{\lambda s^2}{\alpha + (1-\alpha)s} V(r, s) + \lambda d_{2n} \frac{s}{\alpha + (1-\alpha)s} V(r, s) \\ & + d_{2n} V(r, s) - \frac{1}{\text{Re}} \left(\frac{\partial^2 V(r, s)}{\partial r^2} + \frac{1}{r} \frac{\partial V(r, s)}{\partial r} \right) = \left(\frac{h_0}{s} + h_1 \frac{s}{s^2 + \omega^2} - d_{1n} \frac{\omega}{s^2 + \omega^2} \right), \end{aligned} \quad (4.29)$$

$$\text{with } V(1, s) = 0, \frac{\partial V}{\partial r}(0, s) = 0. \quad (4.30)$$

Employing zeroth order finite Hankel transform in Eq. (4.29) with operating BC from Eq. (4.30) yields

$$\begin{aligned} & \left(\frac{s}{\alpha + (1-\alpha)s} + \frac{\lambda s^2}{\alpha + (1-\alpha)s} + \lambda d_{2n} \frac{s}{\alpha + (1-\alpha)s} + d_{2n} \right) V_H(r_n, s) + \frac{r_n^2}{\text{Re}} V_H(r_n, s) \\ & = \left[\frac{h_0}{s} + h_1 \frac{s}{s^2 + \omega^2} - d_{1n} \frac{\omega}{s^2 + \omega^2} \right] \frac{J_1(r_n)}{r_n}, \end{aligned} \quad (4.31)$$

where $V_H(r_n, s) = \int_0^1 r V(r, s) J_0(r_n r) dr$ is the finite Hankel transform of the velocity $V(r, s)$ and

$r_n (n=1, 2, \dots)$ is the positive root of $J_0(\cdot) = 0$ and J_0 is the Bessel functions of order zero and first kind. Rearranging the coefficients of $V_H(r_n, s)$ in Eq. (4.31) yields the following equation:

$$V_H(r_n, s) = \frac{\alpha + (1-\alpha)s}{\lambda s^2 + d_{3n}s + d_{4n}} \left[\frac{h_0}{s} + h_1 \frac{s}{s^2 + \omega^2} - d_{1n} \frac{\omega}{s^2 + \omega^2} \right] \frac{J_1(r_n)}{r_n}. \quad (4.32)$$

Applying the partial fraction decomposition to the right-hand side of Eq. (4.32) gives

$$V_H(r_n, s) = \left(\frac{d_{7n}}{s + d_{5n}} + \frac{d_{8n}}{s + d_{6n}} \right) \left[\frac{h_0}{s} + h_1 \frac{s}{s^2 + \omega^2} - d_{1n} \frac{\omega}{s^2 + \omega^2} \right] \frac{J_1(r_n)}{r_n}. \quad (4.33)$$

Expanding the coefficients of Eq. (4.33), we obtain the following equation

$$V_H(r_n, s) = h_0 \left[d_{7n} \frac{s^{-1}}{s + d_{5n}} + d_{8n} \frac{s^{-1}}{s + d_{6n}} \right] \frac{J_1(r_n)}{r_n} + h_1 \frac{s}{s^2 + \omega^2} \left[d_{7n} \frac{1}{s + d_{5n}} + d_{8n} \frac{1}{s + d_{6n}} \right] \frac{J_1(r_n)}{r_n} - d_{1n} \frac{\omega}{s^2 + \omega^2} \left[d_{7n} \frac{1}{s + d_{5n}} + d_{8n} \frac{1}{s + d_{6n}} \right] \frac{J_1(r_n)}{r_n}. \quad (4.34)$$

The parameters used in simplifying the coefficients of Eqs. (4.10), (4.32) and (4.33) are

$$d_{1n} = \omega h_1 \lambda, \quad d_{2n} = \frac{1 + \text{DaHa}^2}{\text{Da Re}}, \quad d_{3n} = \frac{(1 + \lambda d_{2n}) \text{Re} + (d_{2n} + r_n^2)(1 - \alpha)}{\text{Re}}, \quad d_{4n} = \frac{\alpha (d_{2n} + r_n^2)}{\text{Re}},$$

$$d_{5n} = \frac{(d_{3n} + \sqrt{d_{3n}^2 - 4\lambda d_{4n}})}{2\lambda}, \quad d_{6n} = \frac{(d_{3n} - \sqrt{d_{3n}^2 - 4\lambda d_{4n}})}{2\lambda}, \quad d_{7n} = \frac{\alpha - d_{5n}(1 - \alpha)}{d_{6n} - d_{5n}},$$

$$d_{8n} = \frac{\alpha - d_{6n}(1 - \alpha)}{d_{5n} - d_{6n}}.$$

Inverse Laplace transform of Eq. (4.34) is determined using Robotnov-Hartley $F_\beta(.,.)$ and Lorenzo-Hartley $R_{\beta, \chi}(.,.)$ special functions [75, 76], where

$$F_\beta(-\psi, t) = L^{-1} \left[\frac{1}{s^\beta + \psi} \right] = \sum_{j=0}^{\infty} \frac{(-\psi)^j t^{(j+1)\beta-1}}{\Gamma((j+1)\beta)}, \quad \beta > 0. \quad (4.36)$$

$$\mathfrak{R}_{\beta, \chi}(-\psi, t) = L^{-1} \left[\frac{s^{-\chi}}{s^\beta + \psi} \right] = \sum_{j=0}^{\infty} \frac{(-\psi)^j t^{(j+1)\beta-1-\chi}}{\Gamma((j+1)\beta - \chi)}, \quad \text{Re}(\beta - \chi) > 0. \quad (4.37)$$

$$V_H(r_n, t) = [E_{11n}(t) + E_{22n}(t) + E_{33n}(t)] \frac{J_1(r_n)}{r_n}, \quad (4.38)$$

where

$$E_{11n}(t) = h_0 (d_{7n} \mathfrak{R}_{1,1}(-d_{5n}, t) + d_{8n} \mathfrak{R}_{1,1}(-d_{6n}, t)),$$

$$E_{22n}(t) = h_1 \cos(\omega t) * (d_{7n} F_1(-d_{5n}, t) + d_{8n} F_1(-d_{6n}, t)),$$

$$E_{33n}(t) = -d_{1n} \sin(\omega t) * (d_{7n} F_1(-d_{5n}, t) + d_{8n} F_1(-d_{6n}, t)).$$

with $q_1 * q_2$ shows the Laplace convolution of two functions q_1 and q_2 .

Using inverse HT of order zero to Eq. (4.38), we get

$$V(r, t) = H_0^{-1} V_H(r_n, t) = 2 \sum_{n=1}^{\infty} \frac{J_0(r r_n)}{r_n J_1(r_n)} \times V_H(r_n, t), \quad 0 < \alpha < 1, \quad (4.40)$$

and hence,

$$V(r,t) = 2 \sum_{n=1}^{\infty} \frac{J_0(r r_n)}{r_n J_1(r_n)} [E_{11n}(t) + E_{22n}(t) + E_{33n}(t)]. \quad (4.41)$$

where $J_1(\cdot)$ is the Bessel functions of the first order and first kind.

The volumetric flow rate through cross-sectional area of the vessel can be given by

$$Q(t) = 2\pi \int_0^1 r V(r,t) dr = 4\pi \sum_{n=1}^{\infty} \frac{J_1(r_n)}{r_n^2 J_1(r_n)} [E_{11n}(t) + E_{22n}(t) + E_{33n}(t)]. \quad (4.42)$$

The mean velocity flow field can be written as

$$V_{avg}(t) = \frac{Q(t)}{\pi R_{mv}^2} = 4 \sum_{n=1}^{\infty} \frac{J_1(r_n)}{r_n^2 J_1(r_n)} [E_{11n}(t) + E_{22n}(t) + E_{33n}(t)]. \quad (4.43)$$

4.9.2. Non-invasive procedure of magnetic drug targeting

To determine the trajectories of drug-carrier magnetic nanoparticles in component form we use equilibrium conditions for the motion of the particles. Using Eqs. (4.21), (4.25) – (4.28) into Eq. (4.16), we calculate the velocity components in the $r-z$ plane and get

$$v_{cp,r} = \frac{dr(t)}{dt} = \frac{\mu_0 R_{mv} N_{mp} W_{mp} M_s^2 R_{mag}^4}{8\mu_{nf} A_{cp} k' T} \frac{d_{vm}}{(d_{vm}^2 + z^2)^3} + S, \quad (4.44)$$

$$v_{cp,z} = \frac{dz(t)}{dt} = \frac{\mu_0 R_{mv} N_{mp} W_{mp} M_s^2 R_{mag}^4}{8\mu_{nf} A_{cp} k'} \frac{z}{(d_{vm}^2 + z^2)^3} + V_{avg}. \quad (4.45)$$

where S is the Saffman force parameter given by $S = \frac{6.77 \rho R_{mv} R_{CP}^2 \sqrt{\nu \dot{\gamma}} V_{avg}}{\mu_{nf} A_{CP} k' T}$

$$\text{with } T = 1 + \frac{6.77 \rho R_{mv} R_{CP}^2 \sqrt{\nu \dot{\gamma}}}{\mu_{nf} A_{CP} k'}.$$

The velocity components in Eqs. (4.44) and (4.45) are coupled and can be solved by applying numerical techniques in order to guess the trajectories $(r(t), z(t))$ of drug-carrier magnetic nanoparticles. However, it is also feasible to write the equations independent of each other. Particularly for non-invasive magnetic drug targeting [156],

$$\frac{\mu_0 N_{mp} W_{mp} R_{mv} M_s^2 R_{mag}^4}{8\mu_{nf} A_{cp} k'} \ll 1. \quad (4.46)$$

From the condition of Eq. (4.46), it can be seen that the Saffman force in Eq. (4.44) and fluidic force in Eq. (4.45) are dominant. In this case, the analysis can be simplified by considering that the mean velocity of the drug-carrier magnetic nanoparticles equals the mean blood velocity, and it has the form

$$\bar{v}_{cp,z} = V_{avg} . \quad (4.47)$$

Using this assumption, the axial position of the particles can be written as

$$z(t) = z_0 + V_{avg} t . \quad (4.48)$$

Thus, the axial and radial motions are uncoupled.

Upon substitution of Eq. (4.48) into Eq. (4.45) yields

$$v_{cp,r} = \frac{dr(t)}{dt} = \frac{\mu_0 R_{mv} \beta_{vf} W_{cp} M_s^2 R_{mag}^4}{8 \mu_{nf} A_{cp} k' T} \frac{d_{vm}}{\left(d_{vm}^2 + (z_0 + V_{avg} t)^2 \right)^3} + S . \quad (4.49)$$

where $N_{mp} W_{mp} = \beta_{vf} W_{cp}$, ($0 < \beta_{vf} \leq 1$), β_{vf} is the volume fraction of the drug-carrier magnetic nanoparticles, and $N_{mp} W_{mp}$ is the total volume occupied by the nanoparticles. The position $r(t)$ of the drug-carrier magnetic nanoparticles can be determined from integrating Eq. (4.49)

$$r(t) = r_0 + \frac{\mu_0 R_{mv} \beta_{vf} W_{cp} M_s^2 R_{mag}^4}{8 \mu_{nf} A_{cp} k' T} \int_{t_0}^t \frac{d_{vm}}{\left(d_{vm}^2 + (z_0 + V_{avg} t)^2 \right)^3} dt + \int_{t_0}^t S dt . \quad (4.50)$$

It is important to note that drug-carrier magnetic nanoparticles are captured by magnetic fields, if the traces of drug-carrier magnetic nanoparticles successfully reach the inner wall of the vessel at

$r(t) = -R_{mv}$. The initial position of the drug-carrier magnetic nanoparticles $(r_0, z_0) = (R_{mv}, -4R_{mag})$ is free from the influence of magnetic field, which implies that the drug-carrier magnetic nanoparticles start far away from the tumor region. If the terminal position of the drug-carrier magnetic nanoparticles is at the coordinate $(-R_{mv}, 0)$, i.e., at $z = 0$ and hence

$t = -\frac{z_0}{V_{avg}}$, we say that the drug-carrier magnetic nanoparticles is captured at the left side of the

center of the magnet (i.e., $z \leq 0$). Introducing these conditions into Eq. (4.50), we compute the total volume fraction $\beta_{100,vf}$, which denotes magnetic nanoparticles volume fraction in a drug-

carrier magnetic nanoparticles to ensure the capture of drug-carrier magnetic nanoparticles to the tumor region. Hence,

$$\beta_{100,vf} = \frac{8(2R_{mv} V_{avg} - s z_0) \mu_{nf} A_{cp} k' T}{\mu_0 R_{mv} \beta_{vf} W_{cp} M_s^2 R_{mag}^4 d_{vm}} \left[\frac{\frac{z_0}{4d_{vm}^2 (d_{vm}^2 + z_0^2)^2} + \frac{3z_0}{8d_{vm}^4 (d_{vm}^2 + z_0^2)}}{+ \frac{3}{8d_{vm}^5} \tan^{-1}\left(\frac{z_0}{d_{vm}}\right)} \right]^{-1}. \quad (4.51)$$

4.10. Results and discussion

In the present study, the zeros of Eq. $J_0(x) = 0$, $x \in \mathbb{R}^+$ are used to find the numerical solution of the velocity of a fluid. Eqs. (4.44) and (4.45) represent the trajectories of drug-carrier magnetic nanoparticles in the radial and axial directions, respectively. These equations are coupled and worked out numerically by using the 4th order Runge-Kutta (RK4) method under the initial conditions $z(0) = z_0$ and $r(0) = 1$ at $t = 0$ [127]. In addition, Eq. (4.51) computes the total volume fraction ($\beta_{100,vf}$) of magnetic nanoparticles in drug-carrier magnetic nanoparticles that is expected to confirm capture at the tumor region near the center of the magnet. All computations and simulations were performed by developing a numerical code in MATLAB. The impacts of particle position, fractional parameter α , magnetization parameter M_s , Darcy number Da , Maxwell parameter λ , Saffman force S , shape factor k' on trajectories of drug-carrier magnetic nanoparticles and on the total volume fraction of magnetic nanoparticles are demonstrated. Figs. 4.3 – 4.17 depict the influences of these parameters on the transports of drug-carrier magnetic nanoparticles and on the total volume fraction of magnetic nanoparticles. A set of values for the parameters for the present study is considered from existing literature, and it is shown in Table 4-1. Some of these parameters represent key physical characteristics of blood flow in microvessel. For instance, Reynolds number (Re), Darcy number (Da) and Hematocrit (H_D) are nondimensional parameters that characterize the flow of blood. Besides, the size (R_{mv}) of the blood vessel plays a crucial role in the flow of blood. These flow parameters of blood represent key characteristics of blood behavior and how it interacts with its environment. The values of the parameters indicated are in their normal range which describes proper flow of blood in microvessel. For example, the value of Reynolds number ($Re = 3$) indicates the laminar nature of

blood flow without making any disturbance. For laminar flow of blood in the microvessel, the flow is smooth, with layers of blood flowing parallel to one another without mixing. The hematocrit ($H_D=0.45$) shows the normal percentage of blood volume occupied by red blood cells in the microvessel. Physical conclusions can be drawn from the indicated values of pressure gradient of blood flow parameters (steady amplitude ($h_0 = 0.5 \text{ pa/m}$), amplitude of transient part ($h_1 = 0.6 \text{ pa/m}$) and pulsatile frequency ($\omega = \frac{\pi}{4}$)). In general, the physical meaning of the values of these flow parameters revolves around how the blood moves, how the change in these parameters changes the velocity of blood and trajectory of carrier particles towards the diseased region. Further, the geometry of blood vessel refers to the shape, size, and structural characteristics of blood vessel that influence blood flow. We considered a straight vessel with radius, ($R_{mv} = 50 \mu\text{m}$) because we are dealing with blood flow with carrier particles in the microvessel. The size of carrier particle ($R_{cp} = 200 \text{ nm}$) is the average size that can be influenced by applied magnetic field to reach the target region. The magnetization parameter ($M_s = 10^6 \text{ A/m}$) of the magnet is sufficient to influence the trajectory of carrier particles with the indicated size. Physically, the applied magnetic field couples to the magnetic nanoparticles inside the carrier particle and produces a magnetic force that attracts the particle toward the affected region. The magnet is positioned ($d_{vm} = 0.055 \text{ m}$) from the axis of the microvessel so that the magnetic field sufficiently reaches the region. The volume fraction of magnetic nanoparticles ($\beta_{vf} = 0.28$) is used to ensure at least partial capturing of the drug carrier particles near the tumor region. Moreover, $\mu_0 = 4\pi \times 10^{-7} \text{ N.s/m}^2$ is the permeability of air that allows the magnetic field lines to pass through it with minimum resistance, and $\mu_{\text{plasma}} = 1.2 \times 10^{-3} \text{ N.s/m}^2$ is the viscosity of blood plasma (without the cells and platelets) which is an accepted value at a temperature of 37°C . Furthermore, in our study, we considered the capture of carrier particles with embedded magnetite (Fe_3O_4) nanoparticles with density $\rho = 5000 \text{ kg/m}^3$. Thus, the justifications mentioned above represent the parameters with their corresponding values depicted in Table 4-1.

Table 4 - 1 Physical parameter values with references.

Physical parameters	Values	References
h_0	0.5 Pa/m	Ali et al. [124]
h_1	0.6 Pa/m	Ali et al. [124]
ω	$\pi/4$	Ali et al. [124]
Re	3	Ali et al. [124]
Da	0.8	Yadeta and Shaw [29][127]
φ	0.02	Einstein [53] [149]
H_D	0.45	Furlani and Furlani [156]
R_{mag}	0.03m	Furlani and Furlani [156]
d_{vm}	0.055m	Furlani and Furlani [156]
μ_0	$4\pi \times 10^{-7}$ N.s/m ²	Furlani and Furlani [156]
μ_{plasma}	1.2×10^{-3} N.s/m ²	Furlani and Furlani [156]
β_{vf}	0.28	Furlani and Furlani [156]
M_s	10^6 A/m	Furlani and Furlani [156]
R_{mv}	50 μ m	Furlani and Furlani [156]
R_{CP}	200nm	Furlani and Furlani [156]
ρ	5000 kg/m ³	Furlani and Furlani [152]

4.10.1. Validation

The validation of the present result is in excellent agreement with the Newtonian fluid (Works of [156]) for $\alpha = 1$, $h_0 = 0$, $h_1 = 0$, $\lambda = 0$, $Ha = 0$, $Da \rightarrow \infty$, and the results are shown in Fig. 4.2 and Table 4-2.

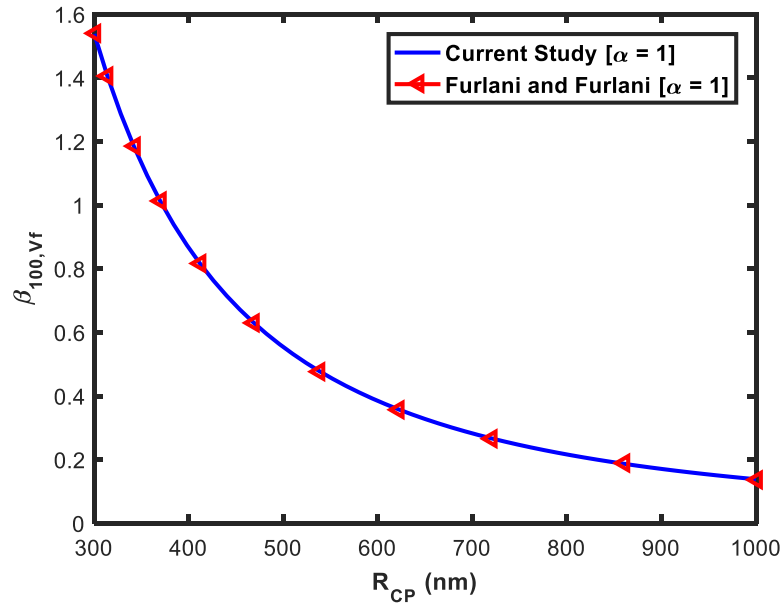


Figure 4-2 A comparison with the work of Furlani and Furlani [156].

Table 4 - 2 A comparison with the work of Furlani and Furlani [156].

Parameters $\alpha = 1, h_0 = 0, h_1 = 0, \lambda = 0, Ha = 0, Da \rightarrow \infty$

R_{CP} (mm)	Furlani and Furlani ($\alpha = 1$)	Current Study ($\alpha = 1$)
300	1.538414	1.538417
370	1.011375	1.011377
440	0.715172	0.715173
510	0.532323	0.532324
580	0.411585	0.411586
650	0.327710	0.327710
720	0.267086	0.267086
790	0.221851	0.221852
860	0.187206	0.187206
930	0.160085	0.160085
1000	0.138457	0.138458

4.10.2. Effects of particle position

The initial positions of drug-carrier magnetic nanoparticles significantly affect the security of the particles near the tumor position during magnetic drug targeting. Fig. 4.3 demonstrates the trajectories of drug-carrier magnetic nanoparticles with different initial positions $(r, z) = (R_{mv}, -4R_{mag})$, where $r = -0.8R_{mv}, -0.6R_{mv}, \dots, 0.8R_{mv}, 1.0R_{mv}$. These initial positions are at the farthest distance from the influence of locally distributed magnetic fields. The axial transport of the drug-carrier magnetic nanoparticles is considered between $z = -4R_{mag}$ and $z = 4R_{mag}$. The magnet is positioned near the tumor region ($z = 0$) at a distance $d_{vm} = 0.055m$ from the axis of the microvessel (Fig. 4.1). From Fig. 4.3, it is observed that particles whose initial radial positions are nearer to the magnet arrive at the diseased region quickly, whereas those particles that start farther away from the magnet are either captured later or escape capture. The phenomena show the prominent role of drug-carrier magnetic nanoparticles position in affecting the capture efficiency of the particles near the tumor region. As we know, drug targeting aims to focus and deliver a high concentration of drug to the targeted region while reducing its concentration elsewhere. Therefore, to achieve this goal, initial drug release locations in the micro vessel is an essential parameter to consider during magnetic drug targeting [156].

4.10.3. Effect of the time-fractional derivative

Blood is a complex fluid in nature due to the occurrence of different blood particles, proteins, plasma, etc. Owing to this reason, the flow behavior of the blood through the microvessel over time is suitably best described by using fractional derivatives. In the present study, we introduced a C-F fractional derivative concept in the momentum equation to describe the flow of blood in the presence of an oscillating pressure gradient and magnetic field. The fractional parameter of a fractional derivative imposes a time memory effect on the flow of blood and on the trajectories of drug carrier particles. The influence of a fractional parameter α on the paths of drug-carrier magnetic nanoparticles and on the total volume fraction of magnetic nanoparticles is displayed in Figs. 4.4 and 4.5, respectively. A wide range of values of parameter α , with $\alpha = 0.7, 0.8, 0.9$, and $\alpha = 1.0$, are considered in the present analysis. The lower value of α ($\alpha = 0.7$) is considered

to have a lower memory impact on the trajectories of drug carriers and on the total volume fraction of magnetic nanoparticles, while the larger value of α ($\alpha = 0.8$ and 0.9) represents a higher memory impact. The value of α with $\alpha = 1.0$ defines the general time derivative has no memory effect.

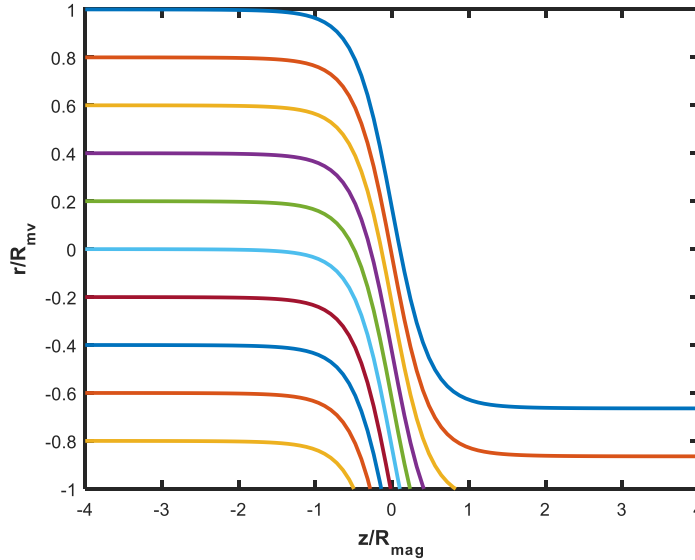


Figure 4.3 Variation of the trajectories of drug-carrier magnetic nanoparticles for different particle positions when $\alpha = 0.8$, $\lambda = 0.2$, $Ha = 1$, $S = 0.5$, $\chi = 2$, and $\gamma = 1.2$.

Fig. 4.4 depicts the trajectories of drug-carrier magnetic nanoparticles in the radial direction with recognition to the axial direction for the alteration of the fractional parameter α . It is important to note that mathematically Eqs. (4.48) and (4.49) are used to predict the trajectory of drug-carrier magnetic nanoparticles ($z(t), r(t)$) given its initial position $(-4, 1)$. From the figure, it is observed that the movement of drug-carrier magnetic nanoparticles is projected toward the arterial wall with an increase in the fractional parameter α . It is ensured that the short memory limits the trajectories of the carrier particle's movement toward the tumor position; however, for the long memory effect and integer order, the drug-carrier magnetic nanoparticles are captured in a good manner. In physical terms, the long memory and integer parameter slow down the velocity of fluid, which in turn facilitates the drop-down of drug-carrier magnetic nanoparticles at the arterial wall where the cancerous tumor is located. On the other hand, the short memory responds quickly to the velocity

of fluid and facilitates the escape of drug-carrier particles from capture. For the larger value of α , the drug-carrier particles get more time span to recall the history of the trajectories and hence drug-carrier particles are easily approached towards the target tumor site. The phenomenon continues for $\alpha = 1.0$ which basically represents the general derivative. It implies that the drug-carrier particles easily reach the tumor region for general form rather than the fractional form.

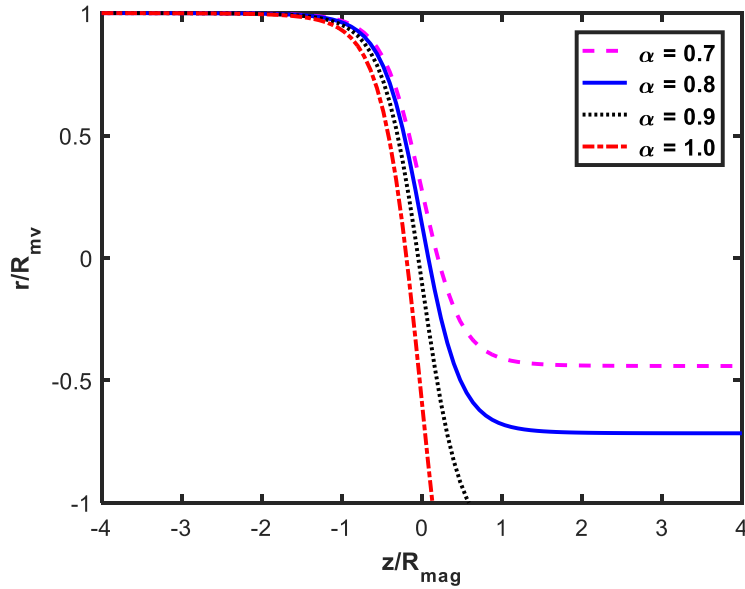


Figure 4.4 Variation of trajectories of drug-carrier magnetic nanoparticles for different α when $\lambda = 0.2$, $Ha = 1$, $S = 0.5$, $\chi = 2$, and $\gamma = 1.2$.

Fig. 4.5 shows the graph of the total volume fraction of magnetic nanoparticles as a function of the radius of drug-carrier magnetic nanoparticles for a variation of the fractional parameter α . It is viewed that the total volume fraction of magnetic nanoparticles declines with a raise in the fractional parameter α , which implies that the smaller total volume fraction for capture requires a higher fractional parameter, which agrees with the result of Fig. 4.4. Further, it is detected that the total volume fraction of magnetic nanoparticles lessens with an improvement in the radius of the drug-carrier particles, which tells us that larger drug-carrier particles require smaller total volume fraction for capture [157], and this dependence can be verified from Eq. (4.51) as total volume fraction is inversely related to the size of drug-carrier particles.

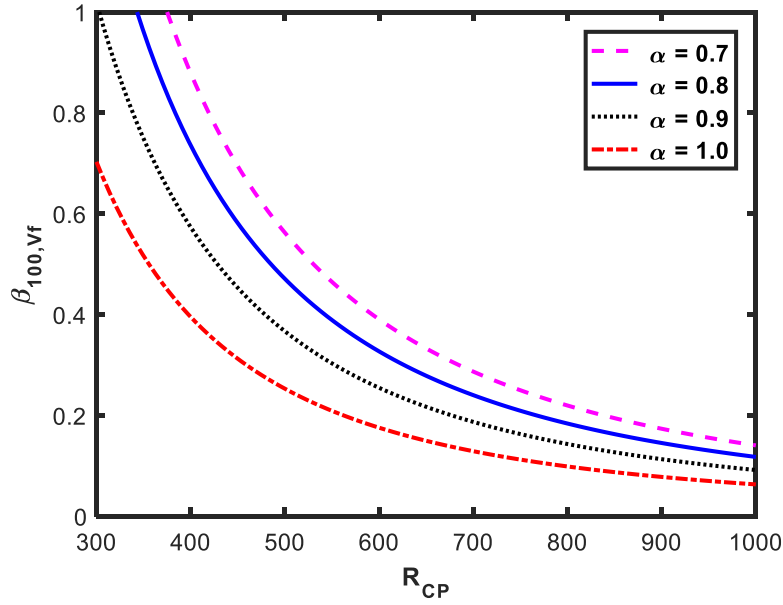


Figure 4.5 Variation of total volume fraction of magnetic nanoparticles $\beta_{100,vf}$ as a function of R_{CP} (nm) for different α when $\lambda = 0.2$, $Ha = 1$, $S = 0.5$, $\chi = 2$, and $\gamma = 1.2$.

4.10.4. Effects of magnetization and particle Size

Fig. 4.6 shows the radial trajectories regarding the axial trajectories of drug-carrier magnetic nanoparticles for different values of the magnetization parameter M_s and the radius of drug-carrier magnetic nanoparticles R_{cp} . Magnetic drug targeting is a non-invasive procedure in which the magnet is placed outside the body near the tumor region and influences the deposition of drug-carrier magnetic nanoparticles. In the present study, we adopt a biocompatible material, a magnetite (Fe_3O_4) nanoparticle embedded in drug-carrier magnetic nanoparticles. For the magnetic field source with magnetization $M_s = 10^6$ A/m, we use a rare-earth NdFeB magnet of radius $0.03m$, positioned at a distance of $0.055m$ from the axis of the blood vessel (see Fig. 4.1) [157]. From Fig.4.6, it is observed that the drug-carrier magnetic nanoparticles are quickly projected towards the arterial wall, with enhancement in the values of M_s . Increasing the magnetization of the magnet increases the accumulation of drug-carrier magnetic nanoparticles near the tumor position. In physical terms, a tumor can develop anywhere in the human body.

Therefore, uplifting magnetization strength can enhance the deposition of particles near the tumor site and achieve high nanoparticle concentrations for deep-seated tumors such as small-cell lung cancer and sarcomas [158, 159]. The size of drug-carrier magnetic nanoparticles is another factor influencing the capture efficiency of drug-carrier magnetic nanoparticles near the tumor region during magnetic drug targeting. In the same figure, it is demonstrated that larger radius of carrier particles facilitates the capture efficiency of drug-carrier magnetic nanoparticles. It is seen that for $R_{cp} = 500 \text{ nm}$, all the drug-carrier magnetic nanoparticles are captured on the left side of the center of the magnet ($z = 0$) for all values of M_s , whereas for $R_{cp} = 100 \text{ nm}$, most of the drug-carrier magnetic nanoparticles escape capture. The ascending size of drug-carrier particles, gives room for more magnetic nanoparticles to be encapsulated, which in turn enhances the intensity of magnetic attraction of drug-carrier particles to the tumor region [157, 158]. Hence, drug-carrier particles for capturing purposes require large particle sizes, which also supports the finding in Section 4.10.3. The discovery presented in Fig. 4.6 will be beneficial to biomedical engineers as they create magnetic devices and the next wave of drug carrier vehicles for diseases such as tumors that are therapy-localized.

4.10.5. Effects of Darcy number & tumor-magnet distance

The effects of Darcy number Da and tumor-magnet distance d_{mv} on the trajectories of drug-carrier magnetic nanoparticles and on the total volume fraction of magnetic nanoparticles are shown in Figs. 4-7 and 4-8, respectively. Porosity and vascular permeability are related properties of the blood vessel, where the latter allows the movement of tiny molecules and cells in and out of the vessel. To demonstrate the impact of varying microvessel permeability on the flow of nanoparticles, we investigated the effect by changing the values of Darcy number. Darcy number Da is associated with the porosity of the arterial wall, and it significantly affects the velocity of the flow field. From Fig. 4.7, it is detected that the capture efficiency of drug-carrier magnetic nanoparticles diminishes near the center of the magnet ($z = 0$) as the vessel permeability increases (ascending Da). In physical terms, increasing Darcy number Da increases the porosity of the arterial wall, which in turn improves the velocity of fluid. A rise in velocity of the fluid pushes away the drug-carrier magnetic nanoparticles and hinders the downward projection of the particles to the diseased region. Hence, it is important to note that an arterial wall with high permeability is

less likely to capture the drug-carrier magnetic nanoparticles. It is reported that the permeability of the microvessel differs from organ to organ such as kidney, brain, lung, liver, and other organs [159]. That is why we have deemed various values of Darcy number Da in the present study. The tumor-magnet distance d between the axis of the microvessel and the edge of the magnet is another physical factor that affects the capture efficiency of drug-carrier magnetic nanoparticles. In the same figure (Fig. 4.7), it is evident that the capture efficiency of drug-carrier magnetic nanoparticles declines with an improvement in tumor-magnet distance. It is evident from Eqs. (4.28) and (4.29) that when the tumor-magnet distance increases, the locally distributed magnetic field influencing the deposition of drug-carrier magnetic nanoparticles decreases and allows the drug-carrier magnetic nanoparticles to escape capture. Hence, drug-carrier magnetic nanoparticles for capture require a smaller tumor-magnet distance. Similar phenomena are noticed in Fig. 4.8 for the total volume fraction $\beta_{100,vf}$ of magnetic nanoparticles. From the figure, it shows that the total volume fraction of magnetic nanoparticles enhances over an increase in Darcy number Da and tumor-magnet distance d . It is evident from the figure that total volume fraction for capture requires a reduced Darcy number and tumor-magnet distance.

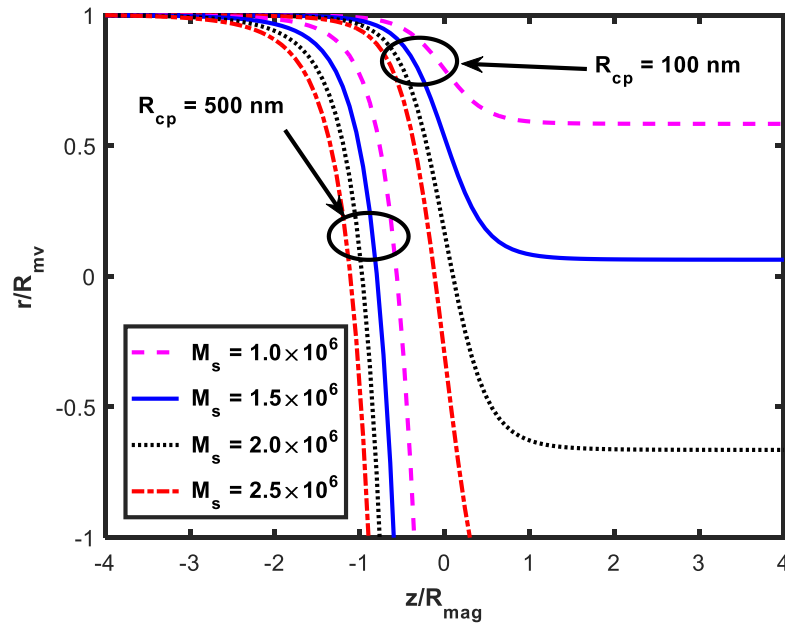


Figure 4.6 Variation of trajectories of drug-carrier magnetic nanoparticles for different M_s and

R_{cp} when $\alpha = 0.8$, $\lambda = 0.2$, $Ha = 1$, $S = 0.5$, $\chi = 2$, and $\gamma = 1.2$.

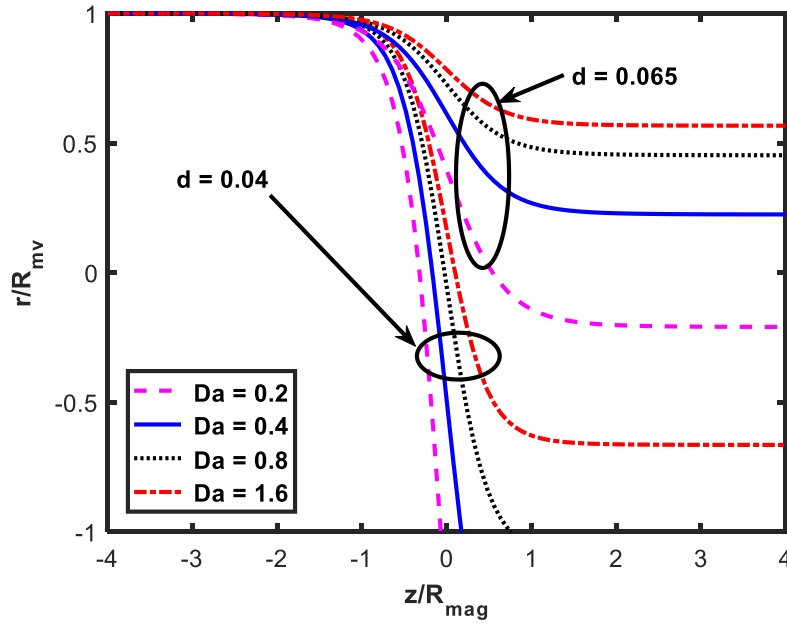


Figure 4.7 Variation of trajectories of drug-carrier magnetic nanoparticles for different Da and d when $\alpha=0.8$, $\lambda=0.2$, $Ha=1$, $S=0.5$, $\chi=2$, and $\gamma=1.2$.

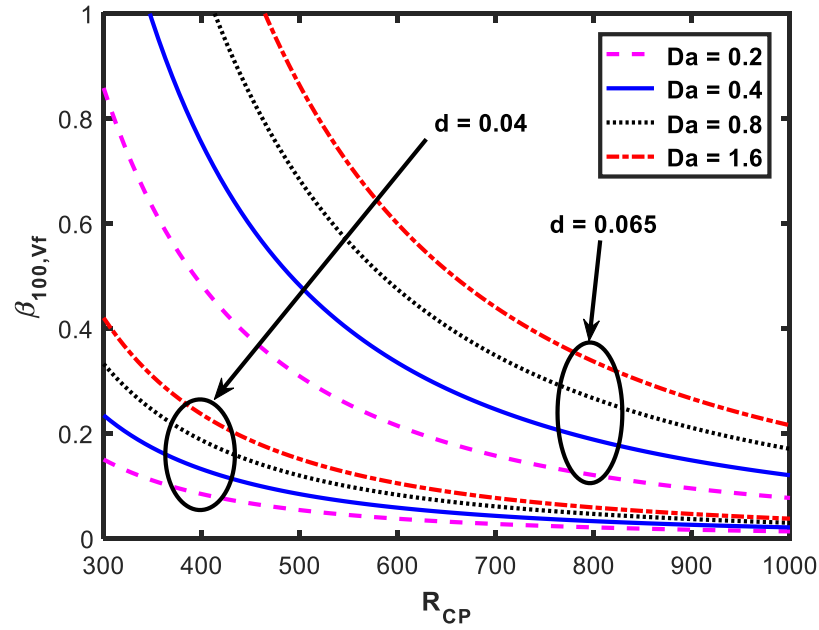


Figure 4.8 Variation of total **volume fraction** of magnetic nanoparticles $\beta_{100,Vf}$ for different Da and d when $\alpha=0.8$, $\lambda=0.2$, $Ha=1$, $S=0.5$, $\chi=2$, and $\gamma=1.2$.

4.10.6. Effects of the Maxwell parameter and Reynolds number

Figs. 4.9 and 4.10 highlights the impacts of Maxwell parameter λ and Reynolds number Re on the radial and axial transports of drug-carrier magnetic nanoparticles with total volume fraction of magnetic nanoparticles, respectively. The Maxwell parameter describes the viscoelastic (elastic and viscous) nature of the fluid, and it is commonly known as relaxation time. From Fig. 4.9, it is detected that the capture efficiency of drug-carrier magnetic nanoparticles declines with an improvement in λ . This happens because the Maxwell parameter has a positive impact on the velocity of fluid, which in turn raises the escape of drug-carrier magnetic nanoparticles from capture. Hence, drug-carrier magnetic nanoparticles for capture require smaller values of the Maxwell parameter. It is crucial to note that the Newtonian rheology ($\lambda = 0$) is better fit for drug-carrier magnetic nanoparticles deposition near the tumor position than the Maxwell rheology ($\lambda = 0.2, 0.3, 0.4$). However, viscoelastic fluids exhibit an interesting property that is not present in Newtonian fluids, like the resonance effect [160]. The difference in the capture efficiency of drug-carrier magnetic nanoparticles in these fluids may be due to the resonance effect. The relation between inertia forces and viscous forces describes the Reynolds number (Re), in which the viscous forces play a significant role in controlling the velocity of the flow field. From Fig. 4.9, it is shown that the possibility of drug-carrier magnetic nanoparticles capture at a particular location decreases with enhancement in Re . It is important to point out that the velocity of fluid improves with an improvement in Re , which in turn restricts the capture of drug-carrier magnetic nanoparticles near the tumor region. For small Re and different values of the Maxwell parameter, the drug-carrier magnetic nanoparticles are totally captured near the center of the magnet. i.e., near the diseased region. Larimi et al. [161] reported that a lower Reynolds number significantly supports the capture efficiency of the particles, which agrees with the present work. Fig. 4.10 plots the total volume fraction $\beta_{100,Vf}$ as a function of R_{CP} to show the impacts of λ and Re on the total volume fraction of magnetic nanoparticles. From the figure, it is shown that the total volume fraction for capture requires small values of λ and Re , which supports the findings of Fig. 4.9.

4.10.7. Effect of the Saffman force and volume fraction

In viscous flow, there are different forces that affect the particle's motion. Among these forces, the Saffman lift force is the shear lift force, which occurs due to the presence of inertia in the

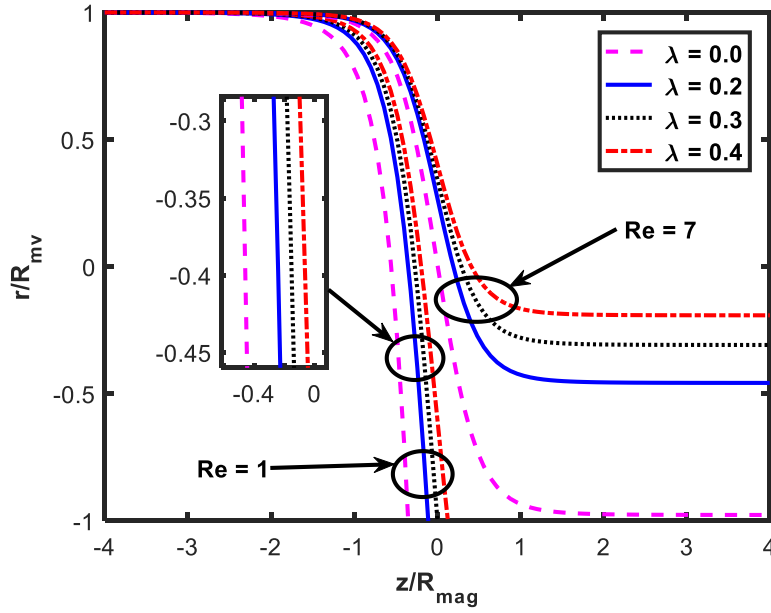


Figure 4.9 Variation of trajectories of drug-carrier magnetic nanoparticles for different λ and Re when $\alpha = 0.8$, $Ha = 1$, $S = 0.5$, $\chi = 2$, and $\gamma = 1.2$.

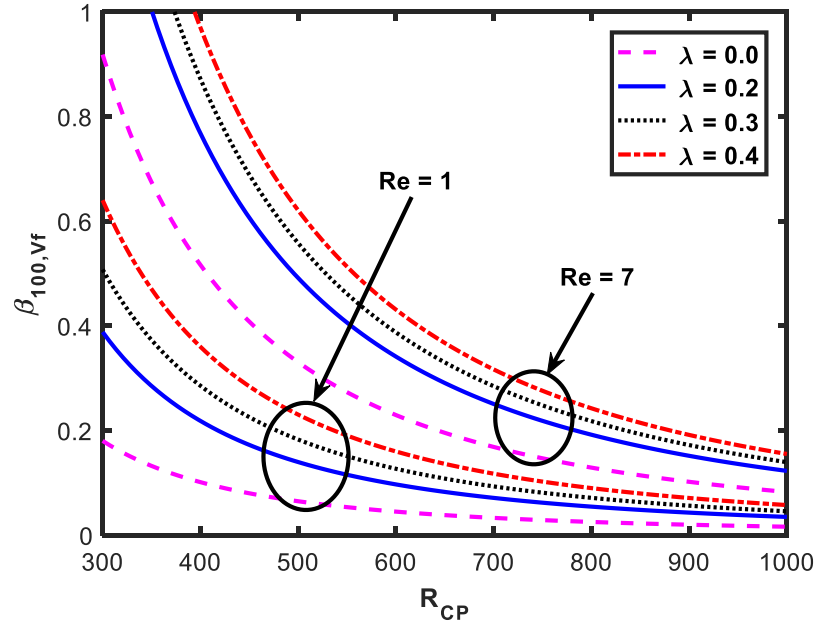


Figure 4.10 Variation of total volume fraction of magnetic nanoparticles $\beta_{100,Vf}$ for different λ and Re when $\alpha = 0.8$, $Ha = 1$, $S = 0.5$, $\chi = 2$, and $\gamma = 1.2$.

viscous flow around the particles. This force plays a significant role during nanoparticle transport in a vessel with a small radius. Zheng and Silber-Li [162] conducted experimental work to see the impact of Saffman lift force on the concentration of nanoparticles moving through a channel of dimensions $55 \times 20 \mu\text{m}$ and 1cm in length. They reported that the Saffman lift force significantly affects the concentration of nanoparticles near the channel wall. Figs. 4.11 is plotted to show the impact of the Saffman force parameter S and volume fraction β_{vf} on the trajectories of drug-carrier magnetic nanoparticles. In order to see the significant effect of Saffman lift force on the trajectories of drug-carrier particles and on the total volume fraction of magnetic nanoparticles, it is assumed that the drug-carrier magnetic nanoparticles are very small in mass and volume. From Fig. 4.11, it is observed that the trajectories of drug-carrier magnetic nanoparticles towards the arterial wall decrease with rise in S . Saffman lift force introduces the drag force in the upward direction, opposing the magnetic field, which attracts the particles to the tumor position. It is also evident from Eq. (4.49) that the Saffman force supports the velocity of drug-carrier magnetic nanoparticles in the radial direction. That is why the increase in Saffman force restricts the trajectories of drug-carrier magnetic nanoparticles to be captured near the tumor region.

The percentage of magnetic nanoparticles in the drug carrier is indicated by the magnetic particle volume fraction. The percentage of magnetic nanoparticles in the drug carrier represents the particle volume fraction. For a constant volume of drug-carrier magnetic nanoparticle, the mass of the magnetic nanoparticles rises with an improvement in the volume fraction. This improves as the volume fraction increases the attraction force between magnetic nanoparticles and a magnet, which in turn facilitates the trajectory of drug-carrier magnetic nanoparticles at the tumor region (see Fig. 4.11). The capture efficiency of drug-carrier magnetic nanoparticles rises with an improvement in volume fraction. It is clearly seen that for a magnetic nanoparticles volume fraction of 80%, the drug-carrier magnetic nanoparticles are fully captured; however, for a volume fraction of 28%, most of the drug-carrier magnetic nanoparticles escape capture. However, the volume fraction of the magnetic nanoparticles is controlled by the presence of the other elements (e.g., drugs) in the drug-carrier particle. The finding shows the prominent advantage of magnetic nanoparticles volume fraction during magnetic drug targeting.

4.10.8. Effect of the shape factor

Fig. 4.12 shows the capture efficiency of drug-carrier magnetic nanoparticles with different shapes near the tumor region, and Fig. 4.13 plots the total volume fraction β_{100, V_f} of magnetic nanoparticles as a function of hematocrit H_D for different shapes of drug-carrier magnetic nanoparticles. The shape of drug carriers potentially influences drug delivery efficiency due to their impact on particle margination and interactions with different cells [159]. The applications of the shapes of drug carriers are beneficial in terms of biocompatibility, pharmacokinetics, targeting, and controlled drug release. Spherical drug carriers, because of their symmetrical nature in shape and easy fabrication, are traditionally used for drug delivery applications [164]. In recent developments, in addition to spherical shaped drug-carrier magnetic nanoparticles, various non-spherical drug-carrier particles with different shapes have been reported. For instance, carriers like oblate ellipsoid, elliptical disk, rectangular disk, UFOs [34], discoidal [165], cylindrical [166], cubic [167], worm-shaped, rod-shaped [168], and others. However, the present study is limited to considering the influences of four different shapes of drug-carrier particles on the trajectories of drug-carrier particles and on the total volume fraction of magnetic nanoparticles. These particles are spherical, circular disc, cylindrical (with $\chi = 2$), and prolate ellipsoidal (with $\gamma = 1.2$). For comparison purposes, we assume that all particles should have the same volume.

From Fig. 4.12, it is observed that except for the circular disc drug-carrier magnetic nanoparticles, all three drug-carrier magnetic nanoparticles are captured effectively near the tumor region, with spherical, prolate ellipsoidal, and cylindrical in order of precedence of capture. The capture efficiency of the spherical drug-carrier magnetic nanoparticles is higher than the other drug-carrier magnetic nanoparticles. This condition may happen because of the symmetric nature of the spherical drug-carrier magnetic nanoparticles, which overcome the fluidic force and are easily being attracted toward the tumor position by a magnet better than the other drug-carrier magnetic nanoparticles. As compared to the other carrier particles, the circular disc drug-carrier magnetic

nanoparticles capture very little. However, despite the lower efficiency of their capture, studies indicated that the disc-shaped drug-carrier magnetic nanoparticles have longer circulation times in the blood stream than the spherical-shaped drug-carrier magnetic nanoparticles. Further, the innate biological system indicates that the non-spherical particles may have a benefit over the spherical particles in sustained circulation time in vivo [169]. In addition to their capture efficiency during drug delivery, drug-carrier magnetic nanoparticles size and shape significantly affects particle circulation time, cellular uptake, bio-distribution, margination, and drug release [164, 170]. Nejati et al. [164], added that the optimum size and shape of a drug-carrier magnetic nanoparticles can be different based on the diseased tissue. Our observation implies that fabricating suitable drug-carrier magnetic nanoparticles size, shape, and surface chemistry can possibly promote accumulation and therapeutic efficacy during drug delivery.

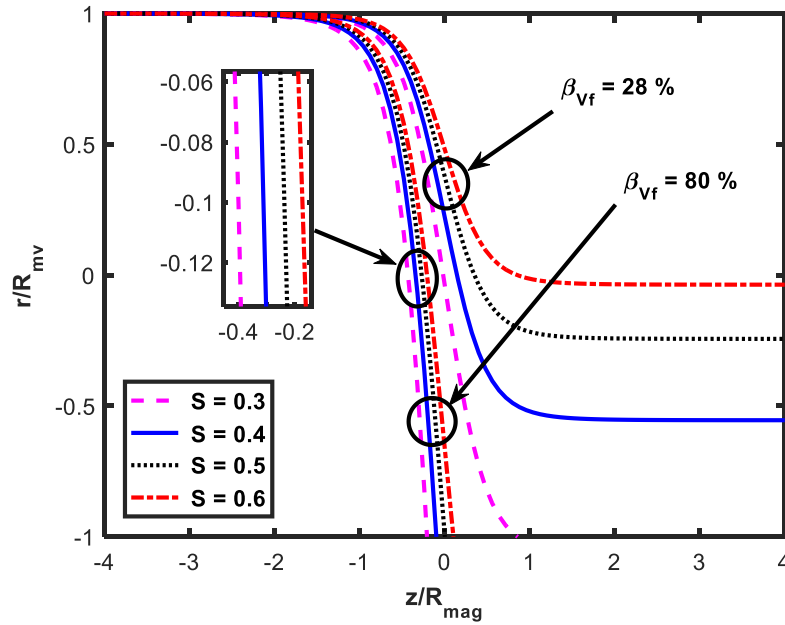


Figure 4.11 Variation of the trajectories of drug-carrier magnetic nanoparticles for different S when $\alpha = 0.8$, $\lambda = 0.2$, $Ha = 1$, $\chi = 2$, and $\gamma = 1.2$.

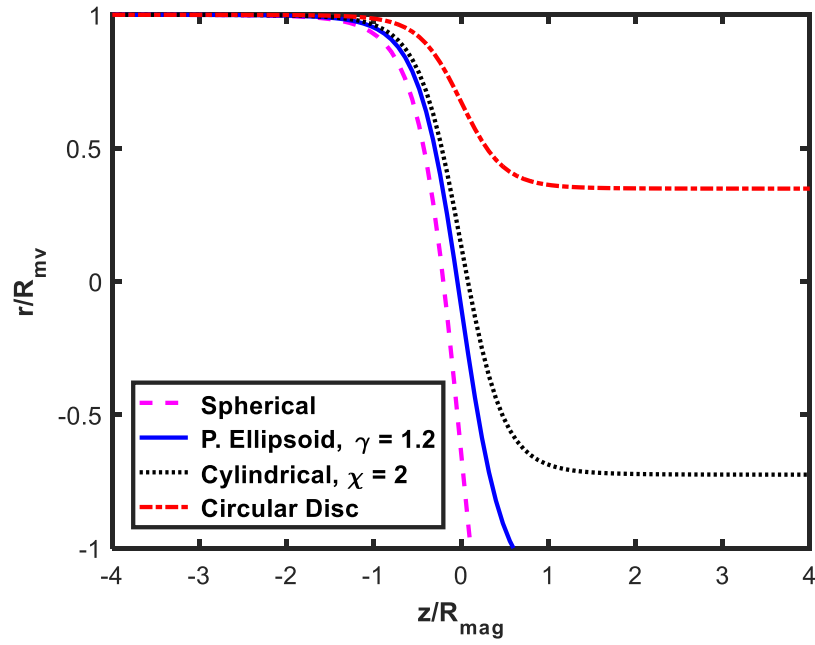


Figure 4.12 Variation of trajectories of drug-carrier magnetic nanoparticles with different shapes of drug-carrier magnetic nanoparticles when $\alpha = 0.8$, $\lambda = 0.2$, $Ha = 1$, and $S = 0.5$.

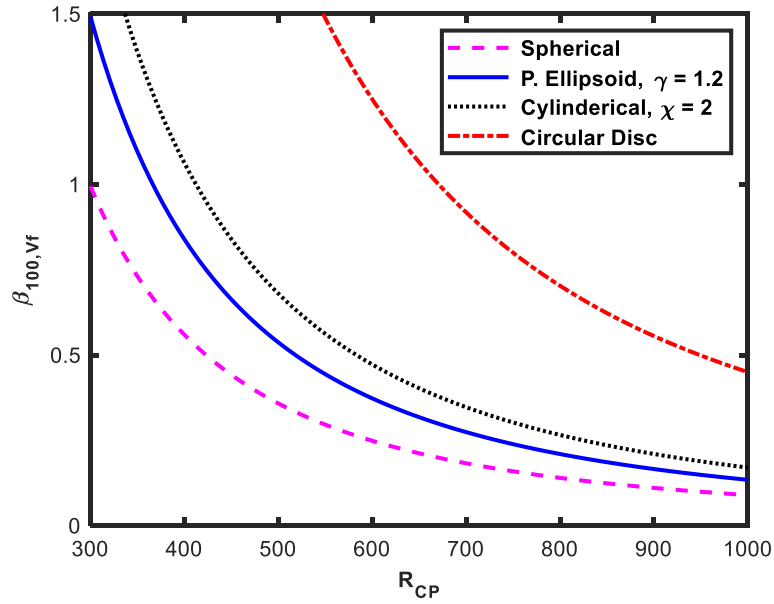


Figure 4.13 Variation of total volume fraction $\beta_{100,Vf}$ of magnetic nanoparticles as a function of H_D for different shapes of drug-carrier magnetic nanoparticles when $\alpha = 0.8$, $\lambda = 0.2$, $Ha = 1$, $S = 0.5$ and $\gamma = 1.2$.

The effect of χ on the trajectories of drug-carrier magnetic nanoparticles and on the total volume fraction β_{100,V_f} of magnetic nanoparticles is shown in Figs. 4.14 and 4.15, respectively. From Fig. 4.14, it is shown that the capture competence of the drug-carrier magnetic nanoparticles decreases with an improvement in the value of χ . This means that when the surface area of the drug-carrier magnetic nanoparticles upsurges, the fluid force acting on the particles increases, which facilitates the escape of the drug-carrier magnetic nanoparticles from capture at the tumor region. The total volume fraction of magnetic nanoparticles enhances with an increase in the value of χ (see Fig. 4.15), which agrees with the findings of Fig. 4.14. Hence, total volume fraction for capture requires a smaller value of χ . Figs. 4.16 and 4.17 depict the impact of γ which shows similar trends to the findings of Figs. 4.14 and 4-15. For $\gamma=1$ implies the spherical shape of the drug-carrier magnetic nanoparticles. It means that efficiency of the drug-carrier magnetic nanoparticles capture at the tumor region decreases when the shape is more non-spherical in shape. The findings from Figs 4.13 – 4.17 will help the nanomedicine researchers develop the next generation of carrier vehicles in different sizes with proper aspect ratio for treatment of cancerous tumors.

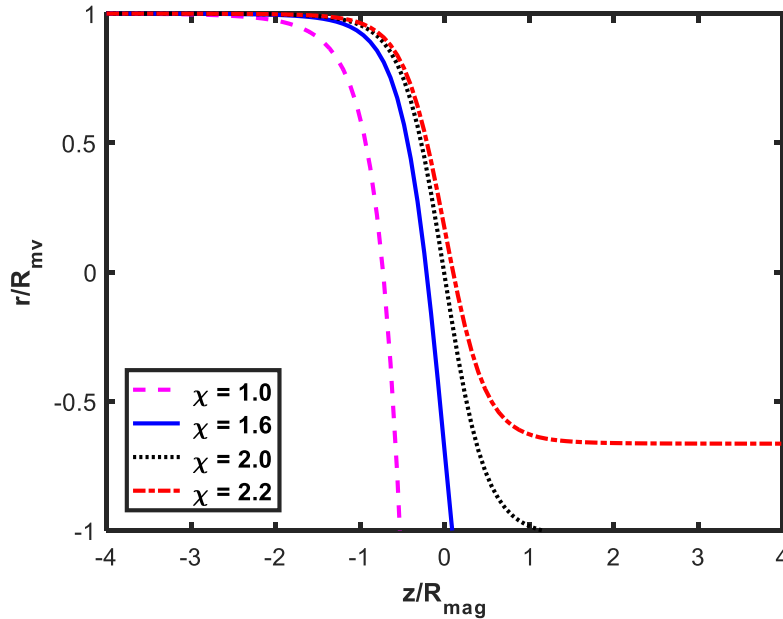


Figure 4.14 Variation of trajectories of drug-carrier magnetic nanoparticles for different χ when $\alpha = 0.8$, $\lambda = 0.2$, $Ha = 1$, $S = 0.5$, and $\gamma = 1.2$.

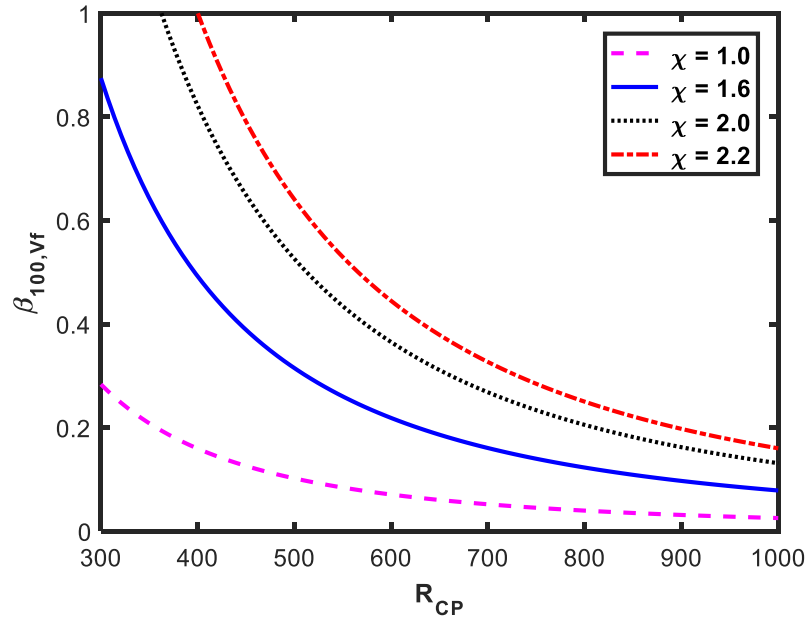


Figure 4.15 Variation of total volume fraction of magnetic nanoparticles $\beta_{100,Vf}$ for different χ when $\alpha = 0.8$, $\lambda = 0.2$, $Ha = 1$, $S = 0.5$, and $\gamma = 1.2$.

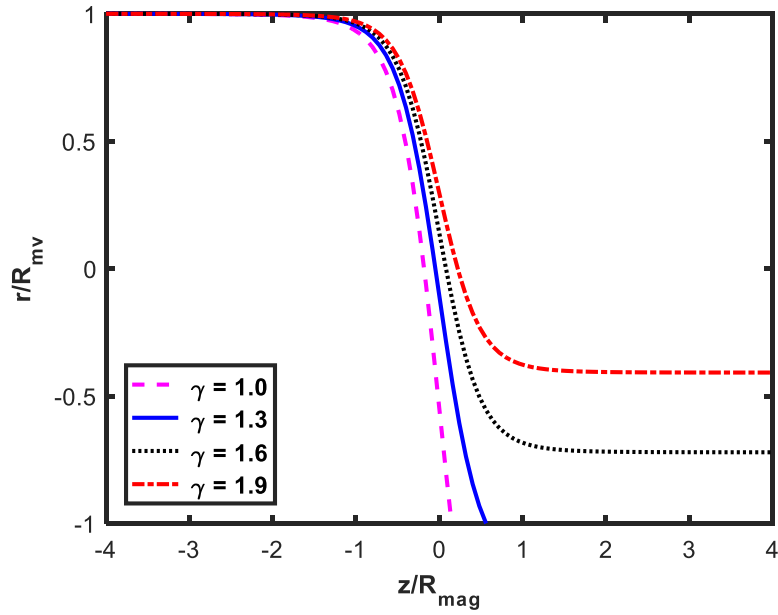


Figure 4.16 Variation of trajectories of drug-carrier magnetic nanoparticles for different γ when $\alpha = 0.8$, $\lambda = 0.2$, $Ha = 1$, $S = 0.5$, and $\chi = 2$.

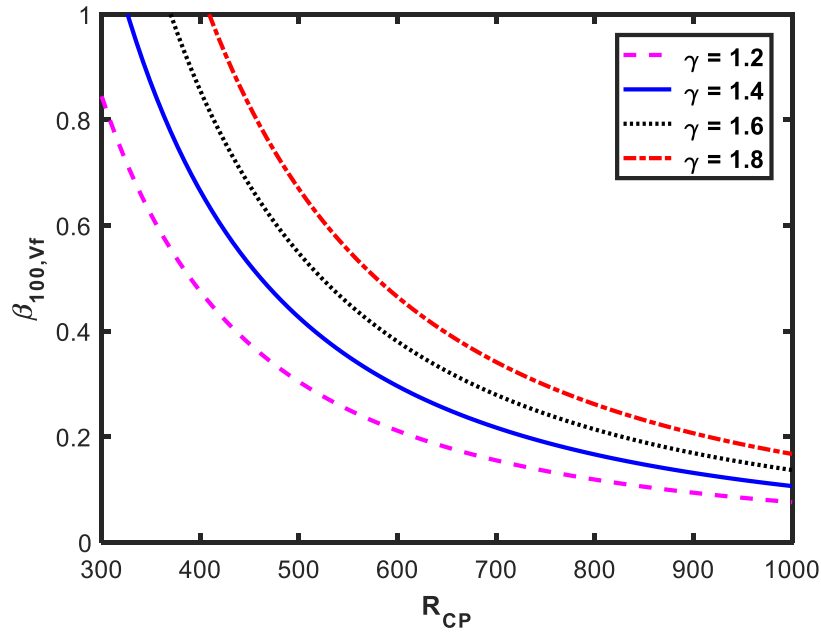


Figure 4.17 Variation of total volume fraction of magnetic nanoparticles $\beta_{100,Vf}$ for different γ when $\alpha = 0.8$, $\lambda = 0.2$, $Ha = 1$, $S = 0.5$, and $\chi = 2$.

4.10.9. Conclusion

The objective of the present model is to analyze the trajectories of drug-carrier magnetic nanoparticles towards the tumor region in a microvessel with Maxwell blood flow during nanoparticle based magnetic drug targeting. We introduced the C-F time fractional model into the momentum equation in order to incorporate the biophysical aspect of the time memory effect. An analytic expression for the average fluid velocity is revealed. The trajectories of drug-carrier magnetic nanoparticles and the total volume fraction of magnetic nanoparticles are obtained numerically using the fourth-order Runge-Kutta (RK-4) method. A significant impact on the trajectories of drug-carrier magnetic nanoparticles and the total volume fraction of magnetic nanoparticles are observed for different controlled parameters such as the particle position, fractional order parameter, magnetization parameter, radius of drug carrier, Darcy number, tumor-magnet distance, Maxwell parameter, Reynolds number, Saffman force parameter, and shape effect. The main findings of the present study are summarized as follows:

- The capture efficiency of drug-carrier magnetic nanoparticles significantly improves when the particle is close to the tumor position as it is easily attracted by the magnet.
- The chance of drug carriers' capture close to the targeted region is more prominent for the larger memory effect (with larger fractional parameter).
- Capture efficiency of the drug-carrier particle is improved with increase in the magnetization, and radius of carrier particles as both increase the magnetic force among the magnet and Drug-carrier particles.
- Maxwell parameters decrease the capture efficiency of the drug-carrier particles due to non-Newtonian viscoelastic nature of blood.
- Lower Darcy number (higher permeability) improves the capture efficiency of the drug-carrier particles as higher permeability lowers the axial velocity of the blood as well as drug-carrier particles.
- Saffman lift force restricted the drug-carrier particles to capture at the tumor region due to introducing additional upward drug force.
- The spherical drug-carrier magnetic nanoparticles capture is higher as compared to the other drug-carrier magnetic nanoparticles capture due to a symmetric nature.
- The total volume fraction required for capture increases with an increase in Darcy number, tumor-magnet distance, Maxwell parameter, Reynolds number, and Saffman force parameter. However, the opposite trend on the total volume fraction is observed for fractional parameters and the radius of drug-carrier magnetic nanoparticles.

The present study has promising applications for treating cancerous tumors and other cardiovascular diseases. In addition, the study will help biomedical engineers and nanomedicine researchers develop the next generation of drug carriers.

5. Magnetic drug targeting during Casson blood flow in a microvessel: A Caputo fractional model[†]

5.1. Introduction

The conventional technique of drug delivery system to the diseased tissue entails the infusion of therapeutic agents to the bloodstream which would be dispersed throughout the patient's body. However, this kind of drug delivery system has significant limitations associated with the nature of free drugs specifically since large dosages of drugs can cause toxicity to healthy tissue [171]. Recently, unlike conventional delivery systems there are some delivery systems to be optimized to target malignant tissue with minimum drawbacks. Among these delivery systems, magnetic drug targeting is a suitable drug delivery mechanism with minimum side effects in which drugs are biocompatible to the healthy tissue, non-invasiveness, and high targeting efficiency [172]. Ndenda et al. [173] presented the impacts of biological parameters on the concentration of drug carrier nanoparticles in microvessels at tumor sites under the application of magnetic field. Analytic solution was presented by [174] to forecast the transportation and capture capacity of magnetic nanoparticles (MNPs) in microvasculature where the process is under noninvasive procedure during magnetic drug targeting. Furlani and Furlani [156] developed a mathematical model to target tumor sites where the movements of therapeutic agents are guided by the dominant external magnetic force. A mathematical model is offered to examine noninvasive magnetic drug delivery systems of multifunctional carrier particles in blood in an impermeable small vessel [175]. Furthermore, various researchers have investigated the behavior of the trajectories of carrier particles (CPs) during drug targeting regarding different circumstances such as rheology of the blood [176, 177] distribution and separate infusion of drug carrier nanoparticles in blood vessel [174], Permeability of microvessel [179], magnetic force [180], and two-phase blood flow mathematical model [181, 182]. Good findings regarding mathematical models on drug targeting can also be found in [183 – 185]. The capture efficiency of particles at a particular location in the existence of a magnetic field also is influenced by various factors such as geometry of the vessel

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[186], vessel shape and particle-particle interactions [187], injection rate of particles and geometry of stenosed vessel [188].

It is worth mentioning that blood flows at a lower shear rate in small blood vessels (arteries) and behaves as non-Newtonian fluid [189]. It is shown that the Casson fluid model is suitable for blood flowing through small vessels with diameter $65\text{ }\mu\text{m} - 500\text{ }\mu\text{m}$ [190–192]. Bali and Awasthi [193] presented the flow of non-Newtonian characteristics of blood in a multi-stenosed circular vessel artery regarding blood as a Casson fluid model. Hayat et al. [194] presented the flow of a Casson fluid model with nanoparticles in a stretching cylinder in the presence of thermal radiation. In general, Blood is a complex fluid, and it contains different blood particles such as Red Blood Cells (RBCs), White Blood Cells (WBCs), platelets, proteins, enzymes etc. Due to their presence, it may not be possible to get information about the past behavior of blood flow when the flow nature is modeled using ordinary time-derivatives. However, the historical information can be obtained by modeling the flow nature using the time-fractional derivative model. Presently, it is observed that many researchers describe the blood flow nature in the form of the fractional derivatives model. Osman et al. [195] presented a time-fractional Caputo derivative model along with Cattaneo's law on Casson fluid flow over a vertical cylinder. Ali et al. [196] demonstrated a time-fractional Caputo derivative model to see the effects of magnetogasdynamics on a two-phase flow of Casson blood and magnetic nanoparticles in a cylindrical vessel in the presence of heat conduction. Ali et al. [197] employed time-fractional Caputo derivative on generalized Casson blood flow with magnetic nanoparticles in the presence of heat conduction. Shah et al. [198] used generalized Fourier and Fick's laws to present a time-fractional Caputo derivative on magnetohydrodynamic flow of Casson nanofluid through an inclined vessel. Ali et al. [124] studied fractional order derivatives to see the effect of non-Newtonian (Casson) fluid flow in axisymmetric circular vessels. Fractional time derivative models are interesting research areas in modeling physical problems due to their memory effect on the outcome solution. To examine the effect of magnetic field, Ali et al. [199] discussed a mathematical model with fractional order for two phase blood flow such that the magnetic nanoparticles in the fluid are with uniform heat transfer. They examined the effect of fractional parameters along with the effect of magnetic field on magnetic nanoparticles flowing in Casson blood using Caputo fractional derivative. Shah et al. [200] presented the impacts of magnetic field and fractional-order parameters on blood flow in a cylindrical vessel by using transformation techniques (Laplace transform (LT) and finite Hankel

transform (FHT) along with their inverse transforms). For more investigations on other time-fractional models we refer a reader to see Refs. [103, 201, 202, 203, 204].

In the afore mentioned literatures, until now no researcher has considered a fractionalized Caputo Casson fluid model for blood flow with drug carrier particles (CPs) during magnetic drug targeting. However, in the current problem, we have presented the trajectories of drug carrier particles towards the cancer region in the presence of external magnet. The present work analyzed the efficiency of the drug carrier particles capture at the tumor region in which Casson fluid is considered as rheology of blood. The analytic solution for the velocity is determined by using Lorenzo-Hartley and Robotnov-Hartely special functions via the methods of Laplace transform and finite Hankel transform with zero order along with their inverse. The trajectory of the drug carrier particles is obtained from the analysis of the force equilibrium of fluidic and magnetic forces using the fourth order Runge – Kutta method. Further, an analytic solution for total volume fraction (TVF) is computed. Finally, the history (memory) effects of fractional parameters on the radial and axial trajectories of the carrier particles as a function of time, and on total volume fraction of magnetic nanoparticles with carrier particles radius have been recorded and displayed graphically. To the best of our knowledge, the current work is unique as it depends on a fractionalized Casson blood model during magnetic drug targeting (MDT).

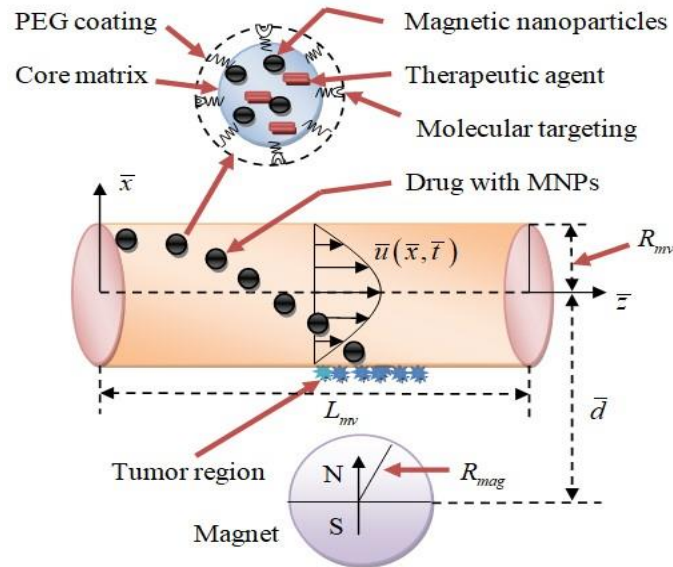


Figure 5.1 Geometrical scheme of trajectories of carrier particles with reference frame.

5.2. Mathematical formulation

Let R_{mv} and L_{mv} be the radius and length of a microvessel, respectively, and assume that the Casson fluid model represents the blood that flows in the horizontal microvessel. We assume that the vertical axis ($\bar{x}$ – axis) is the radial axis and the horizontal axis ($\bar{z}$ – axis) is the axial axis where the vessel is taken along the axial direction. The magnetic nanoparticles in the bloodstream are supposed to be dispersed uniformly. The unsteady Casson fluid flow of blood in axisymmetric cylindrical coordinates $(\bar{x}, \bar{\theta}, \bar{z})$ satisfies the governing momentum equation which is given by

$$\begin{aligned} \frac{\partial \bar{u}}{\partial \bar{t}} = \frac{1}{\rho} [\bar{b}_0 + \bar{b}_1 \cos(\bar{\omega} \bar{t})] + \nu \left(1 + \frac{1}{\beta} \right) \left(\frac{\partial^2 \bar{u}}{\partial \bar{x}^2} + \frac{1}{\bar{x}} \frac{\partial \bar{u}}{\partial \bar{x}} \right) \\ + \bar{A}_0 \cos(\bar{k} \bar{t} + \phi_0) - \frac{\nu}{K_p} \bar{u} - \frac{\sigma B_0^2}{\rho} \bar{u}, \end{aligned} \quad (5.1)$$

where, $-\frac{\partial \bar{p}}{\partial \bar{z}} = \bar{b}_0 + \bar{b}_1 \cos(\bar{\omega} \bar{t})$, $\bar{b}_0$, $\bar{b}_1$, and $\bar{\omega}$ are the oscillating pressure gradient, amplitude of the pressure gradient, amplitude of the pulsatile element rise due to systole and diastole, and pulsatile frequency, respectively [205]. $\bar{A}_0 \cos(\bar{k} \bar{t} + \phi_0)$, $\bar{A}_0$, ϕ_0 , $\bar{k} = 2\pi f_b$, f_b , are the body acceleration, amplitude, lead angle, Stoke's constant, and frequency in Hz, respectively. ρ , ν ,

$\bar{u}$, $\beta = \frac{\mu_\beta \sqrt{\pi_c}}{\tau_y}$, μ_β , τ_y , π_c , σ , and B_0 are the density of fluid, kinematic viscosity, velocity

of fluid, the material parameter of Casson fluid, plastic dynamic viscosity, yield stress of fluid, the critical value of the product based on the non-Newtonian model, electrical conductivity, and applied magnetic field, respectively.

The suitable initial and boundary conditions corresponding to Eq. (5.1) are

$$\bar{u}(\bar{x}, 0) = 0 \text{ for } \bar{t} = 0, \quad \bar{x} \in [0, R_{mv}], \quad \bar{u}(R_{mv}, \bar{t}) = 0, \quad \frac{\partial \bar{u}}{\partial \bar{x}}(0, \bar{t}) = 0, \quad \bar{t} > 0, \quad (5.2)$$

At the initial time $\bar{t} = 0$, the velocity of the fluid is zero, which is indicated by the first initial condition.

In order to make Eq. (5.1) and Eq. (5.2) dimensionless, we introduce [205]

$$\left. \begin{aligned} x &= \frac{\bar{x}}{R_{mv}}, t = \frac{\bar{t}}{\lambda}, u = \frac{\bar{u}}{u_0}, b_0 = \frac{\lambda \bar{b}_0}{\rho u_0}, b_1 = \frac{\lambda \bar{b}_1}{\rho u_0}, \omega = \lambda \bar{\omega}, k = \lambda \bar{k}, A_0 = \frac{\lambda \bar{A}_0}{u_0} \\ z &= \frac{\bar{z}}{R_{mag}}, M_s = \frac{\bar{M}_s}{M_0}, d = \frac{\bar{d}}{R_{mag}}, R_{cp} = \frac{\bar{R}_{cp}}{R_{mv}}, R_{mp} = \frac{\bar{R}_{mp}}{R_{mv}}, \end{aligned} \right\}, \quad (5.3)$$

where R_{mv} , R_{mag} , R_{mp} , u_0 , and M_0 are radius of microvessel, radius of magnet, radius of magnetic nanoparticles, characteristic velocity and magnetization parameter. All these parameters are dimensional parameters. Moreover, the dimension of λ is the same as the dimension of time which we will introduce later to convert the governing equation into a time-fractional Caputo derivative model. Then, Eq. (5.1) can be written as

$$\frac{1}{\lambda} \frac{\partial u}{\partial t} = \frac{1}{\lambda} (b_0 + b_1 \cos(\omega t)) + \frac{\nu}{R_{mv}^2} \left(1 + \frac{1}{\beta} \right) \left(\frac{\partial u}{\partial x^2} + \frac{1}{x} \frac{\partial u}{\partial x} \right) + \frac{1}{\lambda} A_0 \cos(kt + \phi_0) - \frac{\nu}{\kappa_p} u - \frac{\sigma B_0^2}{\rho} u, \quad (5.4)$$

The time-fractional Caputo derivative can be introduced to the governing equation by multiplying Eq. (5.4) by the factor $\lambda = \sqrt{\frac{R_{mv} \rho}{b_0}}$ [124, 200], which results in dimensionless Eq. (5.5)

$$D_t^\alpha u = (b_0 + b_1 \cos(\omega t)) + \frac{1}{\text{Re}} \left(1 + \frac{1}{\beta} \right) \left(\frac{\partial^2 u}{\partial x^2} + \frac{1}{x} \frac{\partial u}{\partial x} \right) + A_0 \cos(kt + \phi_0) - \frac{1}{\text{Da}} u - M^2 u, \quad (5.5)$$

where, $\text{Re} = \frac{R_{mv}^2}{\lambda \nu}$, $\text{Da} = \frac{k_p}{\lambda \nu}$, and $M = B_0 \sqrt{\frac{\lambda \sigma}{\rho}}$, are Reynolds number, Darcy number and

Hartmann number, respectively. The derivative $D_t^\alpha u$ represents the time-fractional Caputo derivative operator of order α with $0 < \alpha < 1$, where

$$D_t^\alpha u(x, t) = \begin{cases} \frac{1}{\Gamma(1-\alpha)} \left(\int_0^t \frac{1}{(t-\tau)^\alpha} \frac{\partial}{\partial \tau} u(x, \tau) d\tau \right), & 0 < \alpha < 1 \\ \frac{\partial u(x, \tau)}{\partial \tau}, & \alpha = 1 \end{cases}, \quad (5.6)$$

The non-dimensional initial-boundary conditions suitable for Eq. (5.5) is given as Eq. (5.7).

$$\left. \begin{aligned} u(x, 0) &= 0 \text{ at } t = 0, x \in [0, 1] \\ u(1, t) &= 0, \frac{\partial u}{\partial x}(0, t) = 0, t > 0 \end{aligned} \right\}, \quad (5.7)$$

5.3. Solution procedure

We solve the governing equation by the concept of integral transforms. First applying the Laplace transform to Eq. (5.5), and using initial condition from Eq. (5.7) we get

$$s^\alpha u(x, s) = \frac{b_0}{s} + b_1 \frac{s}{s^2 + \omega^2} + \frac{1}{\text{Re}} \left(1 + \frac{1}{\beta} \right) \left(\frac{\partial^2 u(x, s)}{\partial x^2} + \frac{1}{x} \frac{\partial u(x, s)}{\partial x} \right) + A_0 \left[\frac{s \cos \phi_0 - k \sin \phi_0}{s^2 + k^2} \right] - \frac{1}{\text{Da}} u(x, s) - M^2 u(x, s) \quad (5.8)$$

$$\text{with } u(1, s) = 0, \frac{\partial u}{\partial x}(0, s) = 0. \quad (5.9)$$

Applying the finite Hankel transform of order zero to Eq. (5.8), and using the boundary condition of Eq. (5.9), we obtain

$$s^\alpha u_H(x_n, s) = -\frac{1}{\text{Re}} \left(1 + \frac{1}{\beta} \right) x_n^2 u_H(x_n, s) - \frac{1}{\text{Da}} u_H(x_n, s) - M^2 u_H(x_n, s) + \left\{ \frac{b_0}{s} + b_1 \frac{s}{s^2 + \omega^2} + A_0 \left[\frac{s \cos \phi_0 - k \sin \phi_0}{s^2 + k^2} \right] \right\} \frac{J_1(x_n)}{x_n} \quad (5.10)$$

where, $u_H(x_n, s) = \int_0^1 x u(x, s) J_0(x x_n) dx$, is the finite Hankel transform of the function $u(x, s)$ and

$x_n, n=1, 2, 3, \dots$ are positive zeros of the Eq. $J_0(x) = 0$, with first kind and zero order Bessel function J_0 .

Rearranging and writing Eq. (5.10) in more suitable form, we obtain

$$u_H(x_n, s) = \left\{ \begin{array}{l} b_0 \left(\frac{s^{-1}}{s^\alpha + a_n} \right) + b_1 \left(\frac{s}{s^2 + \omega^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) + A_0 \cos \phi_0 \left(\frac{s}{s^2 + k^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) \\ -A_0 \sin \phi_0 \left(\frac{k}{s^2 + k^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) \end{array} \right\} \frac{J_1(x_n)}{x_n}, \quad (5.11)$$

$$\text{where, } a_n = \frac{\beta_1 x_n^2 + \text{Re}(1 + \text{Da} M^2)}{\text{Re Da}}, \quad \beta_1 = \left(1 + \frac{1}{\beta} \right).$$

Taking the inverse Laplace transform of both sides of Eq. (5.11), reveals

$$u_H(x_n, s) = \left\{ \begin{array}{l} b_0 L^{-1} \left(\frac{s^{-1}}{s^\alpha + a_n} \right) + b_1 L^{-1} \left(\frac{s}{s^2 + \omega^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) \\ + A_0 \cos \phi_0 L^{-1} \left(\frac{s}{s^2 + k^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) \\ - A_0 \sin \phi_0 L^{-1} \left(\frac{k}{s^2 + k^2} \right) \left(\frac{1}{s^\alpha + a_n} \right) \end{array} \right\} \frac{J_1(x_n)}{x_n}, \quad (5.12)$$

In order to evaluate Eq. (5.12), we use the following special functions.

$$L^{-1} \left[\frac{s^{-\nu}}{s^\alpha + \chi} \right] = R_{\alpha, \nu}(-\chi, t) = \sum_{m=0}^{\infty} \frac{(-\chi)^m t^{(m+1)\alpha-1-\nu}}{\Gamma[(m+1)\alpha-\nu]}, \quad \text{Re}(\alpha-\nu) > 0, \quad (5.13)$$

$$L^{-1} \left[\frac{1}{s^\alpha + \chi} \right] = F_\alpha(-\chi, t) = \sum_{m=0}^{\infty} \frac{(-\chi)^m t^{(m+1)\alpha-1}}{\Gamma[(m+1)\alpha]}, \quad \alpha > 0, \quad (5.14)$$

where, $R_{\alpha, \nu}(-\chi, t)$ and $F_\alpha(-\chi, t)$ are the Lorenzo - Hartley and Robotnov – Hartley functions respectively [75, 76]. Using, Eqs. (5.13) and (5.14) into Eq. (5.12), we obtain

$$u_H(x_n, t) = \left[H_{11n}(t) + H_{22n}(t) + H_{33n}(t) + H_{44n}(t) \right] \frac{J_1(x_n)}{x_n}, \quad (5.15)$$

where,

$$\left. \begin{array}{l} H_{11n}(t) = b_0 R_{\alpha, 1}(-a_n, t), \quad H_{22n}(t) = b_1 \cos(\omega t) * F_\alpha(-a_n, t), \\ H_{33n}(t) = A_0 \cos \phi_0 [\cos(kt) * F_\alpha(-a_n, t)], \quad H_{44n}(t) = -A_0 \sin \phi_0 [\sin(kt) * F_\alpha(-a_n, t)] \end{array} \right\}, \quad (5.16)$$

and $f_1 * f_2$ describes the convolution of Laplace transform with functions f_1 and f_2 .

Applying inverse finite Hankel transform of order zero on Eq. (5.15), the velocity profile can be written as

$$u(x, t) = H_0^{-1} u_H(x_n, t) = 2 \sum_{n=1}^{\infty} \frac{J_0(x x_n)}{J_1^2(x_n)} u_H(x_n, t), \quad (5.17)$$

Upon substitution of the value of $u_H(x_n, t)$ into Eq. (5.17), we get

$$u(x, t) = H_0^{-1} u_H(x_n, t) = 2 \sum_{n=1}^{\infty} \frac{J_0(x x_n)}{J_1^2(x_n)} \left[H_{11n}(t) + H_{22n}(t) + H_{33n}(t) + H_{44n}(t) \right] \frac{J_1(x_n)}{x_n}, \quad (5.18)$$

implies

$$u(x, t) = 2 \sum_{n=1}^{\infty} \frac{J_0(x x_n)}{x_n J_1(x_n)} \left[H_{11n}(t) + H_{22n}(t) + H_{33n}(t) + H_{44n}(t) \right], 0 < \alpha < 1. \quad (5.19)$$

The flow rate of a fluid can be defined as

$$Q = 2\pi \int_0^1 x u(x, t) dx = 4\pi \left[H_{11n}(t) + H_{22n}(t) + H_{33n}(t) + H_{44n}(t) \right] \sum_{n=1}^{\infty} \frac{J_1(x_n)}{x_n^2 J_1(x_n)}. \quad (5.20)$$

The mean fluid velocity can be written as

$$u_f(t) = \frac{Q}{\pi R_{mv}^2} = 4 \left[H_{11n}(t) + H_{22n}(t) + H_{33n}(t) + H_{44n}(t) \right] \sum_{n=1}^{\infty} \frac{J_1(x_n)}{x_n^2 J_1(x_n)}. \quad (5.21)$$

5.3.1. Special case for general derivative ($\alpha = 1$)

For the fractional parameter $\alpha = 1$, the fluid equation follows a general derivative, which reduces Eqs. (5.13) and (5.14) to

$$R_{1,v}(-\chi, t) = \frac{1 - \exp(-\chi t)}{\chi}, F_1(-\chi, t) = \exp(-\chi t), \quad (5.22)$$

and the velocity profile from Eq. (5.17) can be expressed as

$$u(x, t) = 2 \sum_{n=1}^{\infty} \frac{J_0(x x_n)}{J_1^2(x_n)} u_H(x_n, t) = 2 \sum_{n=1}^{\infty} \frac{J_0(x x_n)}{J_1^2(x_n)} [A_{11n}(t) + A_{22n}(t) + A_{33n}(t) + A_{44n}(t)], \quad (5.23)$$

where,

$$\left. \begin{aligned} A_{11n}(t) &= b_0 \frac{1 - e^{-a_n t}}{a_n}, \quad A_{22n}(t) = b_1 \cos(\omega t) e^{-a_n t}, \\ A_{33n}(t) &= A_0 \cos \phi_0 [\cos(kt) e^{-a_n t}], \quad A_{44n}(t) = -A_0 \sin \phi_0 [\sin(kt) e^{-a_n t}] \end{aligned} \right\}. \quad (5.24)$$

The volumetric flow rate and the mean velocity are given as Eqns. (5.25) and (5.26), respectively.

$$Q = 4\pi [A_{11n}(t) + A_{22n}(t) + A_{33n}(t) + A_{44n}(t)] \sum_{n=1}^{\infty} \frac{J_1(x_n)}{x_n^2 J_1(x_n)}, \quad (5.25)$$

$$u_f(t) = 4 [A_{11n}(t) + A_{22n}(t) + A_{33n}(t) + A_{44n}(t)] \sum_{n=1}^{\infty} \frac{J_1(x_n)}{x_n^2 J_1(x_n)}. \quad (5.26)$$

5.4. Effective viscosity of fluid

Effective viscosity is based on the hematocrit of the blood (volume fractions of RBCs) which highly influences the microvessel. The empirical formula for viscosity can be written as [206]

$$\mu = \mu_{plasma} \left[1 + (\mu_{0.45} - 1) \frac{(1 - H_D)^C - 1}{(1 - 0.45)^C - 1} \left(\frac{D_v}{D_v - 1.1} \right)^2 \right] \left(\frac{D_v}{D_v - 1.1} \right)^2, \quad (5.27)$$

where $\mu_{plasma} = 0.0012 N.s / m^2$, D_v , and H_D are the viscosity of blood plasma (without the blood cells and platelets), diameter of the blood vessel in micron, and hematocrit (normally 0.45), respectively.

$$\mu_{0.45} = 6^{-0.085 D_v} + 3.2 - 2.44 e^{-0.06 D_v^{0.645}}, \quad (5.28)$$

$$C = (0.8 + e^{-0.075 D_v}) \left(\frac{1}{1 + 10^{-11} D_v^{12}} - 1 \right) + \frac{1}{1 + 10^{-11} D_v^{12}}. \quad (5.29)$$

5.5. Fluidic force

Blood is characterized as a non-Newtonian fluid because of the presence of low shear stress mainly when the diameter of the vessel is less than 1300 μm . The fluidic force applied on the carrier particles in a laminar flow of Casson fluid is written as

$$F_f = -6\pi\mu \left(1 + \frac{1}{\beta}\right) R_{cp} (v_{cp} - u_f(x, t)), \quad (5.30)$$

where β , R_{cp} and v_{cp} are the Casson parameter, radius of the carrier particles and reference velocity, respectively. The component forms of the fluidic force in the x - z plane can be written as Eq. (5.31) and Eq. (5.32).

$$F_{fx} = -6\pi\mu \left(1 + \frac{1}{\beta}\right) R_{cp} v_{cp,x}, \quad (5.31)$$

$$F_{fz} = -6\pi\mu \left(1 + \frac{1}{\beta}\right) R_{cp} (v_{cp,z} - u_f). \quad (5.32)$$

5.6. Force due to external magnet

We have used effective dipole moment to calculate the force of magnet on the drug carrier particles and it can be written as [174],

$$\bar{F}_f = \mu_f \bar{V}_{mp} \frac{3(\chi_p - \chi_f)}{(\chi_p - \chi_f) + 3(\chi_f + 1)} (H_a \cdot \nabla) H_a, \quad (5.33)$$

where H_a , $\chi_p = \mu_p / \mu_0 - 1$, $\chi_f = \mu_f / \mu_0 - 1$, and μ_f are the applied magnetic field intensity at the center of the nanoparticles, susceptibility of the particles, susceptibility and the permeability of the fluid, respectively. Furthermore, μ_p and μ_0 represents the permeability of the particles and air, respectively. The volume of a spherical magnetic nanoparticles can be written as $\bar{V}_{mp} = \frac{4}{3} \pi \bar{R}_{mp}^3$.

We considered the noninvasive procedure during magnetic drug targeting, where the radius of the microvessel is much less than the distance between drug carrier particle and axis of the magnet ($\bar{d}$). i.e., $\bar{d} \gg R_{mv}$. In addition, we adopt the material of magnetic nanoparticles iron-oxide

(Fe_3O_4), magnetite which is biocompatible [174]. These two assumptions simplify Eq. (5.33), and yield the components of the magnetic force in the $\bar{x} - \bar{z}$ plan as

$$\bar{F}_{mx}(\bar{x}, \bar{z}) = -3\mu_0 \bar{V}_{mp} \bar{M}_s^2 R_{mag}^4 \frac{\bar{d}}{2(\bar{d}^2 + \bar{z}^2)^3}, \quad (5.34)$$

$$\bar{F}_{mz}(\bar{x}, \bar{z}) = -3\mu_0 \bar{V}_{mp} \bar{M}_s^2 R_{mag}^4 \frac{\bar{z}}{2(\bar{d}^2 + \bar{z}^2)^3}, \quad (5.35)$$

where R_{mag} , $\bar{M}_s$ and $\bar{z}$ represents the radius of magnet, magnetic parameter and the axial distance of carrier particles, respectively.

Using dimensionless parameters from Eq. (5.3) into Eqs, (5.34) and (5.35), we get

$$F_{mx}(x, z) = \Gamma \beta_{vf} R_{cp}^3 M_s^2 \frac{d}{(d^2 + z^2)^3}, \quad (5.36)$$

$$F_{mz}(x, z) = \Gamma \beta_{vf} R_{cp}^3 M_s^2 \frac{z}{(d^2 + z^2)^3}, \quad (5.37)$$

where $\Gamma = -\frac{2\pi\mu_0 M_0^2 R_0^3}{R_{mag}}$.

5.7. Equation of motion

Furlani and Ng [174] pointed out that magnetic force, fluidic force, inertia force, buoyancy force, gravity force, particle-blood/cell interactions, interparticle effects and particle-fluid interactions are some factors involved in magnetic drug targeting. Among these forces magnetic and fluidic forces are dominated more in the magnetic drug targeting [156]. Further, for microvessel, particle-blood-cell interaction plays a significant role by improving the viscosity of the blood. In the present problem, we mainly focus on the above three factors. Particle-particle interactions (Brownian motion) and particle-fluid interactions are ignored due to a small particle volume concentration ($\ll 1$) in the blood streaming during magnetic drug targeting.

Therefore, the transport of drug carrier particles can be calculated using Newton's second law of motion as

$$m_{cp} \frac{dv_{cp}}{dt} = F_m + F_f, \quad (5.38)$$

where, m_{cp} , v_{cp} , F_m , F_f represents particle mass, particle velocity, magnetic force, and fluidic force, respectively. The force term $m_{cp} \frac{dv_{cp}}{dt} \approx 0$, because m_{cp} is very small due to the radius of the particles which is in nanoscale [156, 185].

The final form of the force balance reduces to

$$F_m + F_f = 0, \quad (5.39)$$

5.8. Trajectories of carrier particles under noninvasive procedure

In noninvasive magnetic drug targeting, the treatment took place without any break of the skin and controlled from outside of the body, which leads to the condition

$$\frac{\Gamma \beta_{vf} R_{cp}^2 M_s^2}{6\pi\mu} \ll 1, \quad (5.40)$$

Using Eqs. (5.31), (5.32), (5.36) and (5.37) into (5.39), we obtain the velocity components for the carrier particles in the $x-z$ plane as

$$v_{cp,x} = \Gamma \frac{\beta_{vf} R_{cp}^2 M_s^2}{6\pi\mu \left(1 + \frac{1}{\beta}\right)} \frac{d}{(d^2 + z^2)^3}, \quad (5.41)$$

$$v_{cp,z} = \Gamma \frac{\beta_{vf} R_{cp}^2 M_s^2}{6\pi\mu \left(1 + \frac{1}{\beta}\right)} \frac{z}{(d^2 + z^2)^3} + u_f, \quad (5.42)$$

The axial location of the drug carrier particles is given by

$$z = z_0 + v_{cp,z} t, \quad (5.43)$$

The velocities u_f and $u_{cp,z}$ (average blood velocity and carrier particles velocity, respectively) are supposed to be equal, and hence

$$u_{cp,z} = u_f, \quad (5.44)$$

With help of Eqs. (5.41) - (5.44), the trajectories of carrier particles $x(t)$ and $z(t)$ can be written, respectively as

$$\frac{dx(t)}{dt} = \Gamma \frac{\beta_{vf} R_{cp}^2 M_s^2}{6\pi\mu \left(1 + \frac{1}{\beta}\right)} \frac{d}{\left(d^2 + (z_0 + u_f t)^2\right)^3}, \quad (5.45)$$

$$\frac{dz(t)}{dt} = \Gamma \frac{\beta_{vf} R_{cp}^2 M_s^2}{6\pi\mu \left(1 + \frac{1}{\beta}\right)} \frac{z_0 + u_f t}{\left(d^2 + (z_0 + u_f t)^2\right)^3} + u_f. \quad (5.46)$$

To determine the total volume fraction of magnetic nanoparticles that ensures the capture capacity of carrier particles, we integrate Eq. (5.45) and get

$$x(t) = x_0 + \int_{t_0}^t \Gamma \frac{\beta_{vf} R_{cp}^2 M_s^2}{6\pi\mu \left(1 + \frac{1}{\beta}\right)} \frac{d}{\left(d^2 + (z_0 + u_f t)^2\right)^3} dt, \quad (5.47)$$

In the present study it is worth mentioning that, if the trajectories of drug carrier particles reach the inner wall of the microvessel at $x(t) = -R_{mv}$, we say that the particle is captured by a magnetic field. The coordinate $(x_0, z_0) = (R_{mv}, -4R_{mag})$ is the initial position of the carrier particle where the magnetic force is initially negligible. i.e., the carrier particles start far away at the upstream of the magnet. If the particle is to be captured above the center of the magnet (i.e., $z = 0$), then its terminal position should be $x(t) = R_{mv}$ at $z = 0$, i.e., when $t = -\frac{z_0}{u_{cp,z}}$. We substitute these

conditions in Eq. (5.47) and compute the total volume fraction $\beta_{vf,100}$ ($0 < \beta_{vf,100} \leq 1$), which

represents the magnetic nanoparticles volume fraction in a carrier particles that is needed to guarantee its capture below or above the center of the magnet i.e., $z \leq 0$ [154, 177].

$$\beta_{vf,100} = \frac{12\pi\mu\left(1+\frac{1}{\beta}\right)u_f R_{mv}}{\Gamma R_{cp}^2 M_s^2 d} \left[\frac{z_0}{4d^2(d^2+z_0^2)^2} + \frac{3z_0}{8d^4(d^2+z_0^2)} + \frac{3}{8d^5} \tan^{-1}\left(\frac{z_0}{d}\right) \right]^{-1}. \quad (5.48)$$

5.9. Results and discussion

Solve relation $J_0(x) = 0$ numerically to find the positive roots and consider at least one for finding the velocity profile. In the present study, the trajectories of the carrier particles are determined from Eqs. (5.45) and (5.46) that involve different biological parameters. Since Eqs. (5.45) and (5.46) are extremely coupled and hence, solve numerically (fourth-order RK method) with the initial conditions $z(t) = z_0$ at $t = 0$ and $x(t) = 1$ at $t = 0$. Furthermore, Eq. (5.48) is used to calculate the magnetic nanoparticles total volume fraction $\beta_{vf,100}$ in carrier particles that is needed to ensure its capture at the tumor region.

The present work is compared with the works of Furlani and Furlani [156] for $\alpha = 1$, $Da \rightarrow \infty$, $\beta \rightarrow \infty$, $M \rightarrow 0$, $A_0 = b_1 = 0$ with Newtonian rheology of blood and it has been displayed in Fig. 5-2 and Table 5-1, and the results are found to be in a very good agreement. The effects of the physical parameters namely the magnetic parameter (Ms), Darcy number (Da), Reynolds number (Re), pulsatile frequency (ω), and fractional parameter (α), on the radial and axial trajectories, and on the total volume fraction of magnetic nanoparticles are presented. Moreover, the impacts of tumor-magnet distance (d), Casson parameter (β) and Hematocrit parameter (H_D) on total volume fraction of magnetic nanoparticles are demonstrated. For the rest of numerical computations, the parameter values considered are $b_0 = 0.6$, $b_1 = 0.5$, $A_0 = 0.5$, $\phi_0 = 0.4$, $k = 0.3$, $Da = 0.8$, $Re = 5$, $\beta = 0.6$, $H_D = 0.45$. Impact of the Caputo fractional time derivative on the trajectories of drug carrier particles in axial and radial direction with total volume fraction of the magnetic nanoparticles is depicted in Figs. 5.3 – 5.17.

5.9.1. Impact of time-fractional derivative

The time-memory depicts the condition in which fluid properties change over time. In the present work, we incorporated the time-memory effect in the governing equation by applying a Caputo fractional time derivative. The history of the trajectories of carrier particles, and total volume fraction of magnetic nanoparticles in the fluid can easily be observed with fractional order time derivative. Based on the nature of the trajectories of drug carrier particles history, it is possible to predict their current behavior. However, a future prediction of drug carrier particles is possible in the absence of particle-particle and particle-fluid interaction forces. In the present investigation, we considered three different values of fractional parameters ($\alpha = 0.6, 0.8, 0.9$) and one ordinary parameter ($\alpha = 1$). $\alpha = 0.6$ and $\alpha = 0.9$ are used to describe short and long-time memory effects respectively, whereas the value $\alpha = 1$ represents the classical first order derivative with no memory effect on the trajectories of carrier particles and volume fraction. This observable fact discloses a good understanding of the force balance with the memory effect.

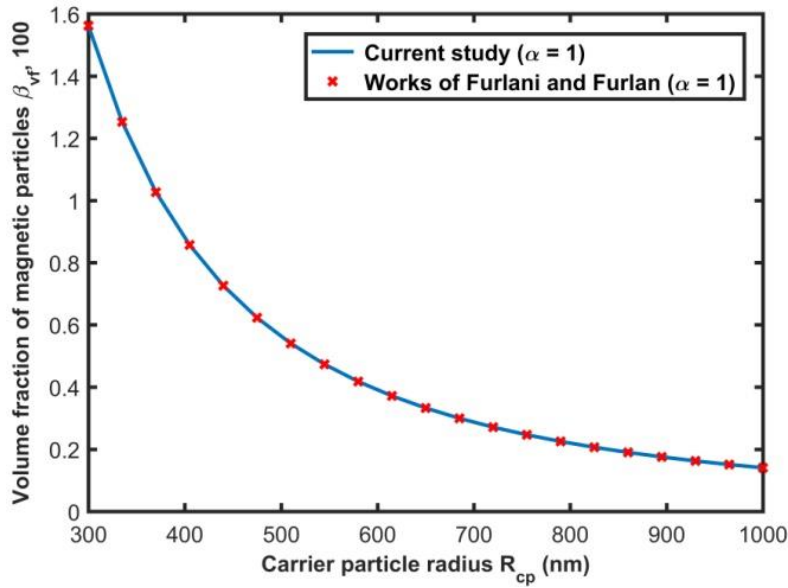


Figure 5.2 A comparative result with Furlani and Furlani [156].

Table 5 - 1 A comparison with the work of Furlani and Furlani [156].

Parameters $\alpha = 1, Da \rightarrow \infty, \beta \rightarrow \infty, M \rightarrow 0, A_0 = b_1 = 0$		
R_{cp} (mm)	Furlani and Furlani [156] ($\alpha = 1$)	Current Study ($\alpha = 1$)
300	1.538414	1.538417
370	1.011375	1.011377
440	0.715172	0.715173
510	0.532323	0.532324
580	0.411585	0.411586
650	0.327710	0.327710
720	0.267086	0.267086
790	0.221851	0.221852
860	0.187206	0.187206
930	0.160085	0.160085
1000	0.138457	0.138458

From Figs. 5.3 and 5.4, we see that the memory effect strongly influences the projection of radial and axial trajectories of drug carrier particles, respectively. Fig. 5.3 depicts that for a short time memory effect it takes less time for the carrier particles to reach the microvessel wall (arterial wall), and it takes a long time for carrier particles to reach the wall when the time memory effect is large. Furthermore, for a large time t , the memory has sufficient time to trace back the initial history of the trajectories of carrier particles. In addition, the current result reveals more important evidence than the normal capture efficiency. Fig. 5.4 shows that for short memory effect ($\alpha = 0.6$), the axial trajectories of carrier particles travel longer distances whereas long-time memory effect ($\alpha = 0.9$) restricted the travel at a particular point of time. Figs. 5.6 and 5.9 present the effects of different values of Darcy number (Da) and Reynolds number (Re), along with the memory effect on the radial trajectory of carrier particles.

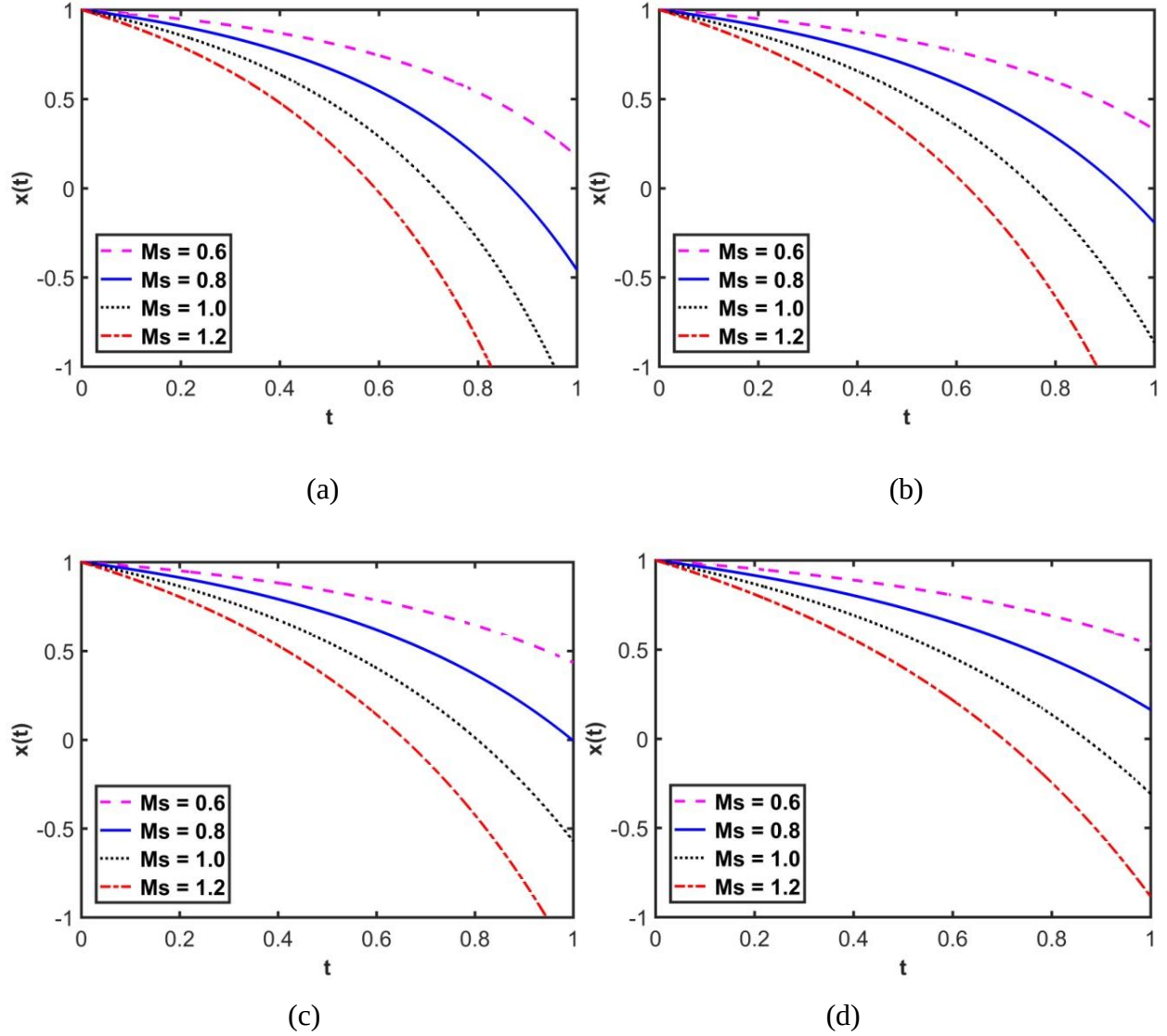


Figure 5.3 Radial trajectories of carrier particles profile for different Ms when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1.0$.

Fig 5.6 shows the carrier particles are quickly captured under the influence of magnetic field for short time memory effect whereas for long time memory effects, the capture capacity delays. For various values of Re the same conclusion can be drawn from the behavior of the solutions (Fig.5.9). Figs. 5.7 and 5.10 illustrate the axial trajectories of drug carrier particles with time under the application of magnetic field for different values of Darcy number (Da) and Reynolds number (Re). The figures show that, for short memory effect, the trajectories of drug carrier particles move longer distances to reach the target site. Figs. 5.5, 5.8, 5.11, 5.14, 5.15, 5.16 and 5.17 depict the

effect of magnetization (Ms), Darcy number (Da), Reynold's number (Re), pulsatile frequency (ω), tumor-magnet distance (d), Casson parameter (β), Hematocrit parameter (H_D), along with the time memory effect on the total volume fraction of magnetic nanoparticles that ensures the capture capacity of carrier particles where $0 < \beta_{vf,100} \leq 1$.

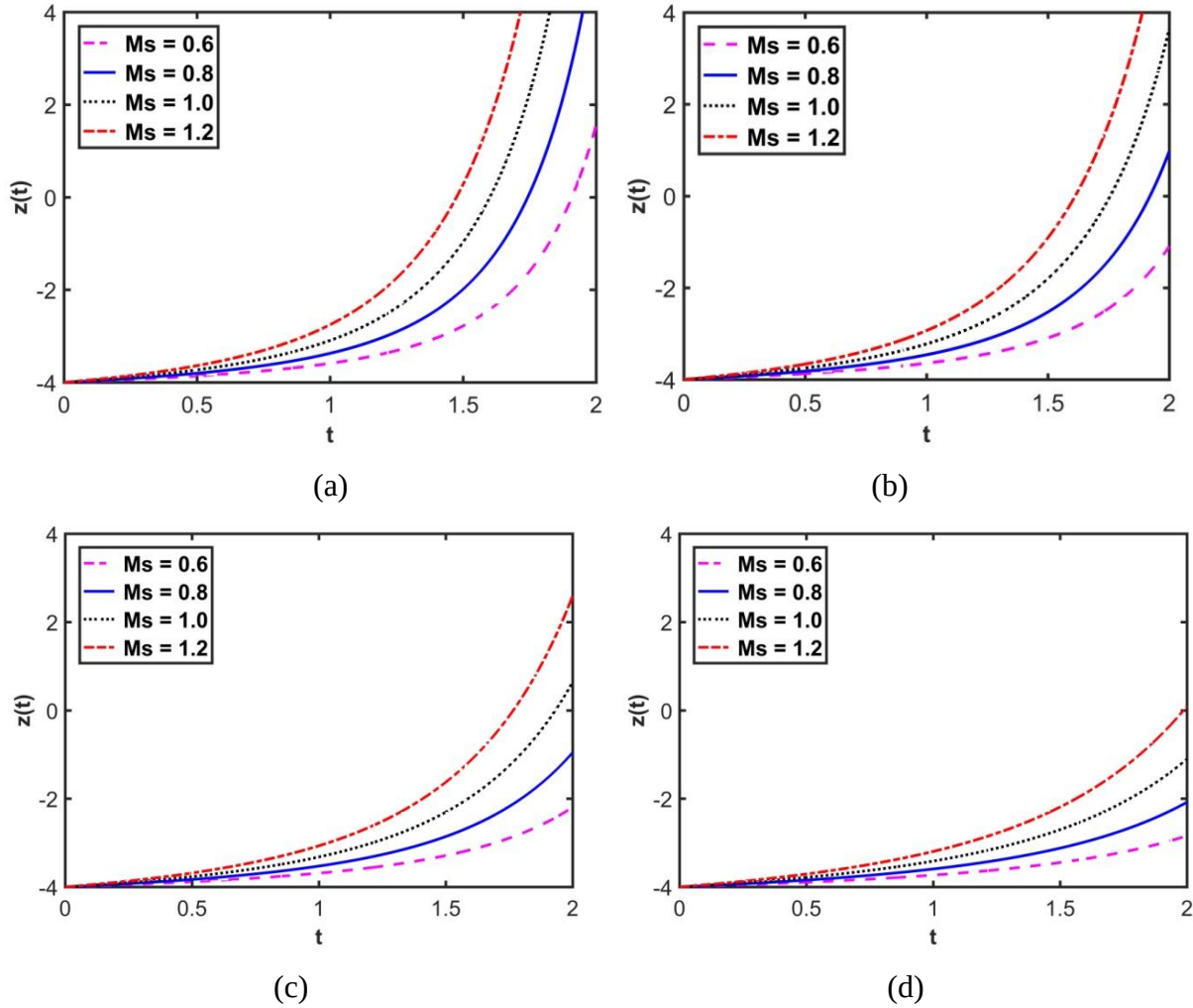


Figure 5.4 Axial trajectories of carrier particles profile for different Ms when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1.0$.

When the total volume fraction is equal to one, the total volume of carrier particles without drugs is fully occupied by magnetic nanoparticles. On the other hand, there are no magnetic nanoparticles inside the carrier particles when the total volume fraction is equal to zero. From the figures it can be seen that for large memory effects and integer order derivatives, the carrier particles are more

quickly captured at the tumor position than for short memory effects. The fractional order parameters reveal a significant effect on the total volume fraction of magnetic nanoparticles and the movement of the drug carrier particles with respect to time. Hence, impact of α is very significant which gives an idea on memory effect during developed a new phenomenon on drug targeting and further provide information during magnetic drug targeting by controlling the movement of the drug carrier particles.

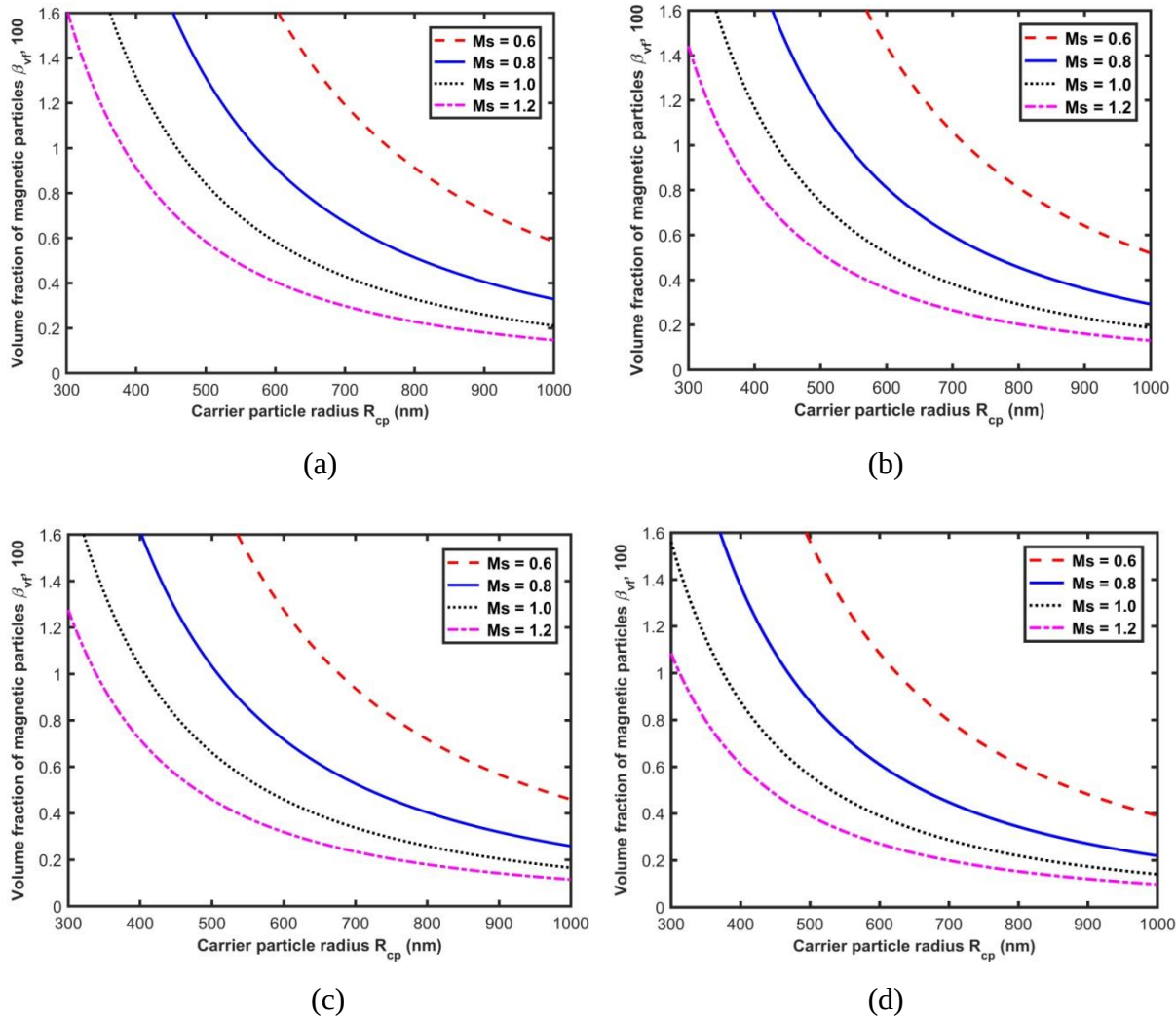


Figure 5.5 Profile of total volume fraction ($\beta_{vf,100}$) vs. R_{cp} for various M_s when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1$.

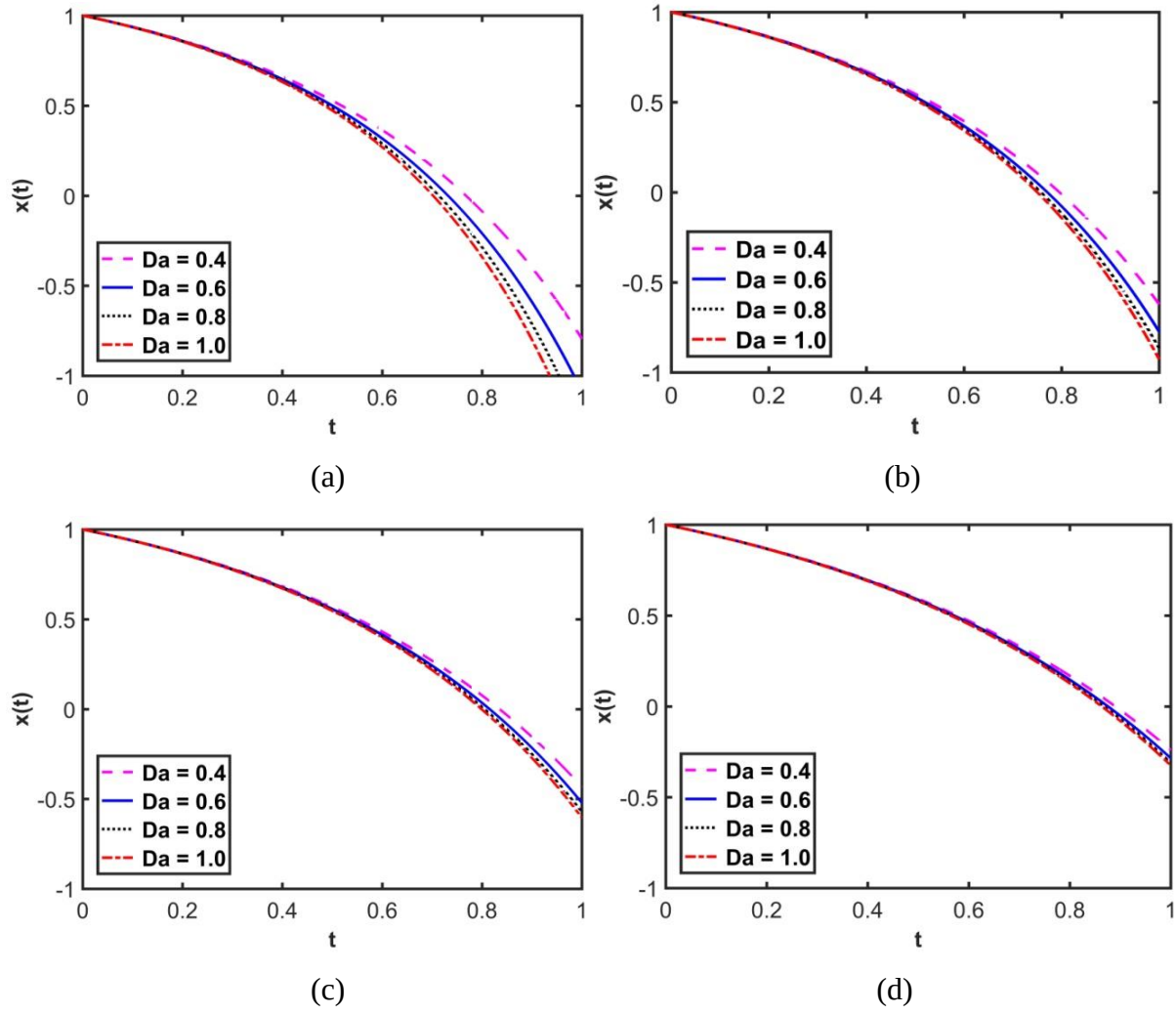


Figure 5.6 Radial trajectories of carrier particles profile for different Da when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1.0$.

5.9.2. The effect of magnetization

It is worth mentioning that magnetization plays an important role during magnetic drug targeting. Increasing magnetization enhances the capture capacity of drug carrier particles at the tumor site. In this study, a magnetization model measured for magnetite (Fe_3O_4) is presented by Furlani and Furlani [152]. A NdFeB magnet of diameter 6 cm (i.e., $R_{mag} = 0.03m$) is considered to create the magnetic field with a dimensionless magnetization $Ms = 1$ (while in dimensional form $Ms = 10^6 A/m$). The magnet is located at a distance of 0.025m from the axis of the microvessel. That is the distance between the axis of magnet and microvessel. Figs. 5.3, 5.4, and 5.5,

demonstrate the impacts of various values of Ms on the projection of trajectories of carrier particles and total volume fraction of magnetic nanoparticles, respectively. The values of nondimensional magnetization considered in this study are $Ms = 0.6, 0.8, 1, 1.2$. From Fig. 5.3, we see that the downward projection of the radial trajectories to the target site boosts up with enhancement in magnetization parameter. However, the condition in the axial trajectories of carrier particles happens to be opposite as we see from Fig. 5.4. From Fig. 5.5 we see that with enhancement in the magnetic parameter, the total volume fraction of magnetic nanoparticles decreases. In this case, the possibility of capture for the carrier particles at the tumor position enhances with ascending magnetization.

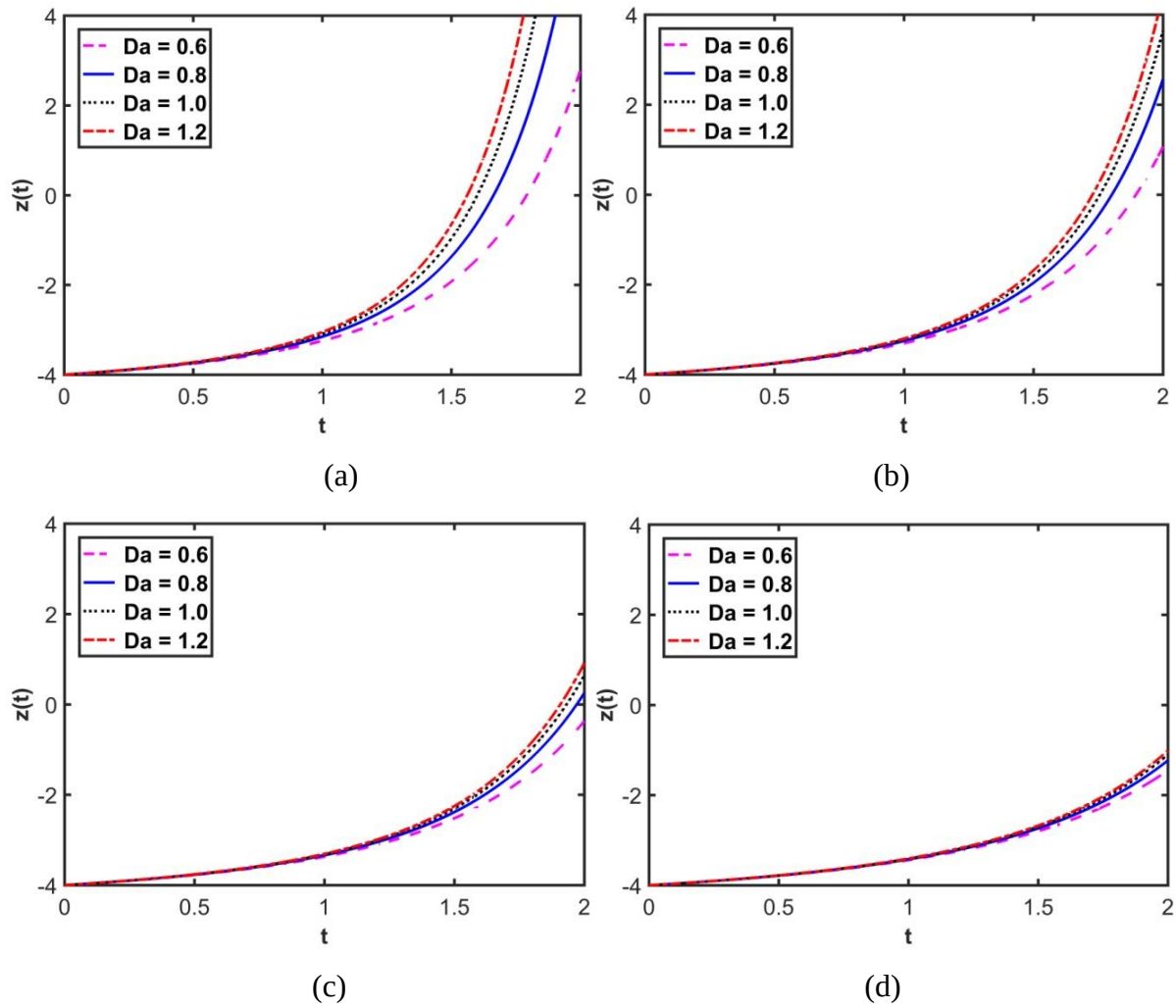


Figure 5.7 Axial trajectories of carrier particles profile for different Da when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1$.

5.9.3. Impact of Darcy number

A Darcy number plays a crucial role in controlling the axial velocity of blood flow and hence it significantly impacts on the magnetic drug targeting. Figs. 5.6 and 5.7 show the effect of Darcy number (Da) on the radial and axial trajectories of drug carrier particles along with time. Fig. 5.8 expresses the impact of Da on total volume fraction of magnetic nanoparticles for capturing purposes. From Fig. 5.6 we see that an increase in Da gears up the radial trajectories of drug carrier particles towards the tumor position. Hence, the magnetic nanoparticles reach faster at the diseased region for large Darcy number. The current work is also supported by the works of Bali et al. [171].

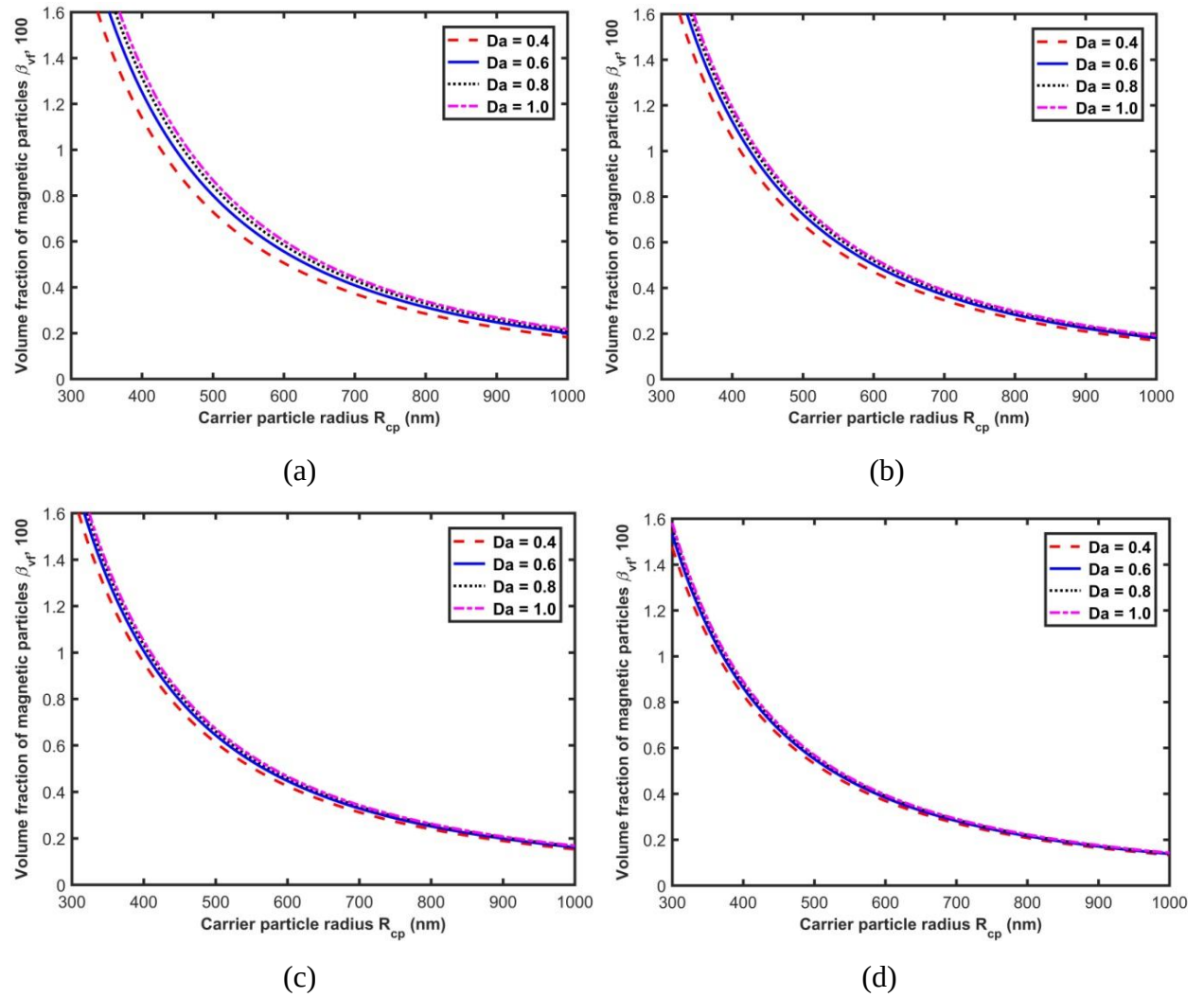


Figure 5.8 Profile of total volume fraction ($\beta_{vf,100}$) vs. R_{cp} for various Da when (a) $\alpha = 0.6$
(b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1$.

In addition, an increase in the porosity parameter boosts up the axial trajectories of the carrier particles (Fig. 5.7). However, it is reported that fluid flow towards the axial direction is restricted by the improved porosity of the wall of the blood vessel [202]. On the other hand, as Darcy number decreases the total volume fraction of nanoparticles decreases.

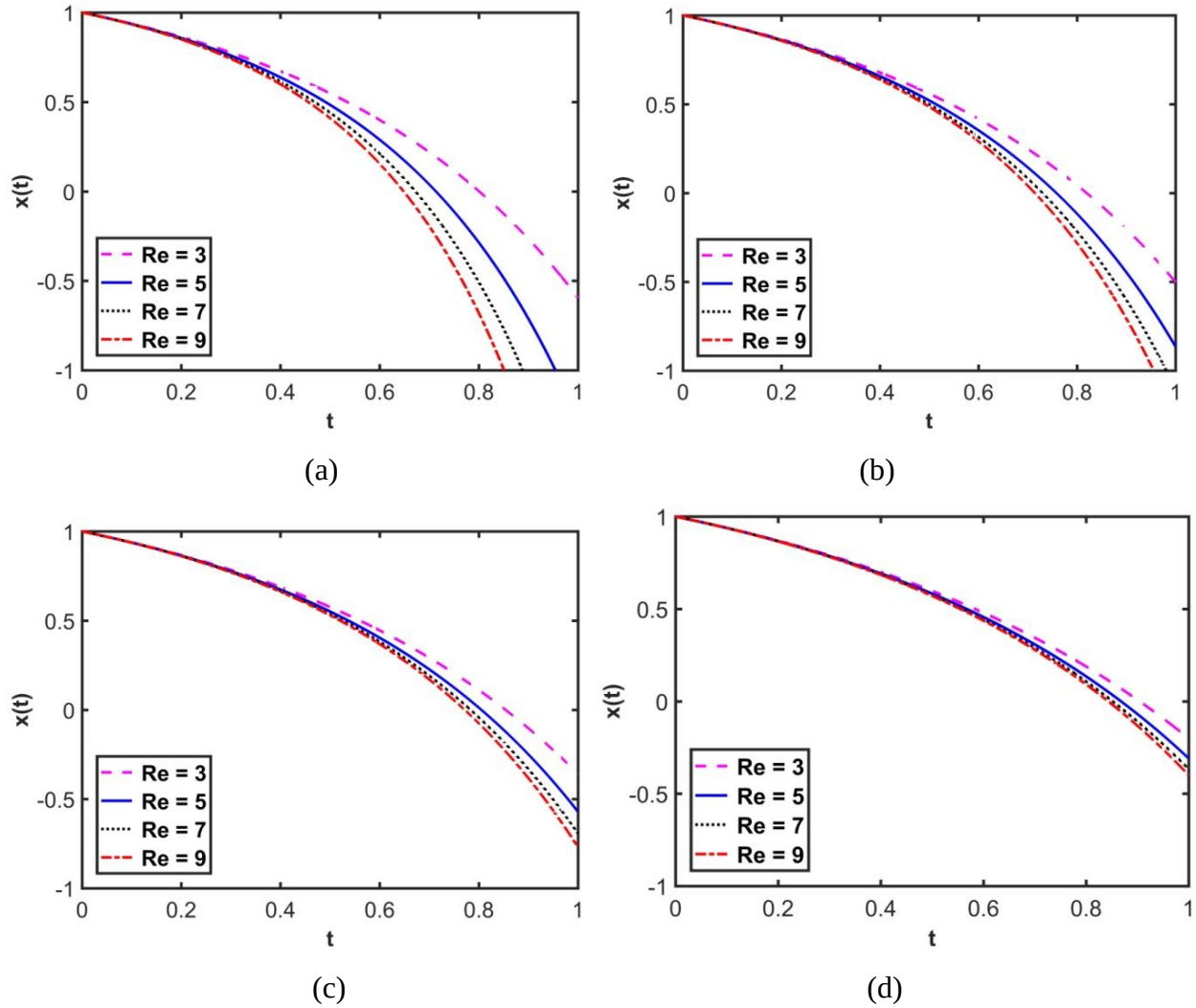


Figure 5.9 Radial trajectories of carrier particles profile for different Re when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1$.

It is worth mentioning that particle size and volume fraction for capture needs a smaller Darcy number during magnetic drug targeting as displayed in Fig. 5.8. It is important to note that the porosity of the microvessel differs with the position of the specific vessel in the organ. In general, it is observed that the porosity nature of the blood vessel is lower in the brain and highly significant

in the glomerulus of the kidney. This implies magnetic drug targeting is more successful at treatment of diseased tissues in the kidney with respect to the brain. However, this is not the only parameter that affects the motion of the trajectories of the drugs carrier particles. Magnetic drug targeting is observed as equally important to cure the tumor in the brain [207].

5.9.4. Impact of Reynolds number

The effect of Reynolds number (Re) with variation of time on the radial and axial trajectories of the carrier particles is depicted in Figs. 5.9 and 5.10, respectively. In this study the Reynolds number used is $Re = 3, 5, 7, 9$. From Fig 5.9, it is demonstrated that the radial trajectories of the drug carrier particles move faster to the microvessel wall with enhancements in Reynolds number. Hence the trajectories of carrier particles towards the tumor position and support with increase in Reynolds number. On the other hand, Fig. 5.10 shows the trajectories of carrier particles move longer distances with enhancement in Reynolds number. It is because an improvement in Reynolds number gears up the fluid's axial velocity which in turn enhances the axial velocity of the drug carrier particles. In the present study, the velocity of the carrier particles is assumed to be equal to the average fluid velocity. The carrier particles move away from the microvessel wall (tumor region) with enhancement in the axial velocity; caused by an increase in fluidic force as shown in Fig. 5.10.

The influence of Reynolds number on the total volume fraction of magnetic nanoparticles with radius of carrier particles in the x - z plane is shown in Fig. 5.11. From Fig. 5.11 it is depicted that the total volume fraction of magnetic nanoparticles increases with enhancement in Reynolds number. This happens due to the fact that increasing Reynolds number increases the axial velocity of carrier particles which in turn increases the total volume fraction of carrier particles. Therefore, in particular, the blood vessels with small Reynolds number are observed to be more impactful and supportive to cure cardiovascular disorders with the help of magnetic drug targeting. Further,

in this case small carrier particles size is observed sufficient to be captured at the tumor region with small Re.

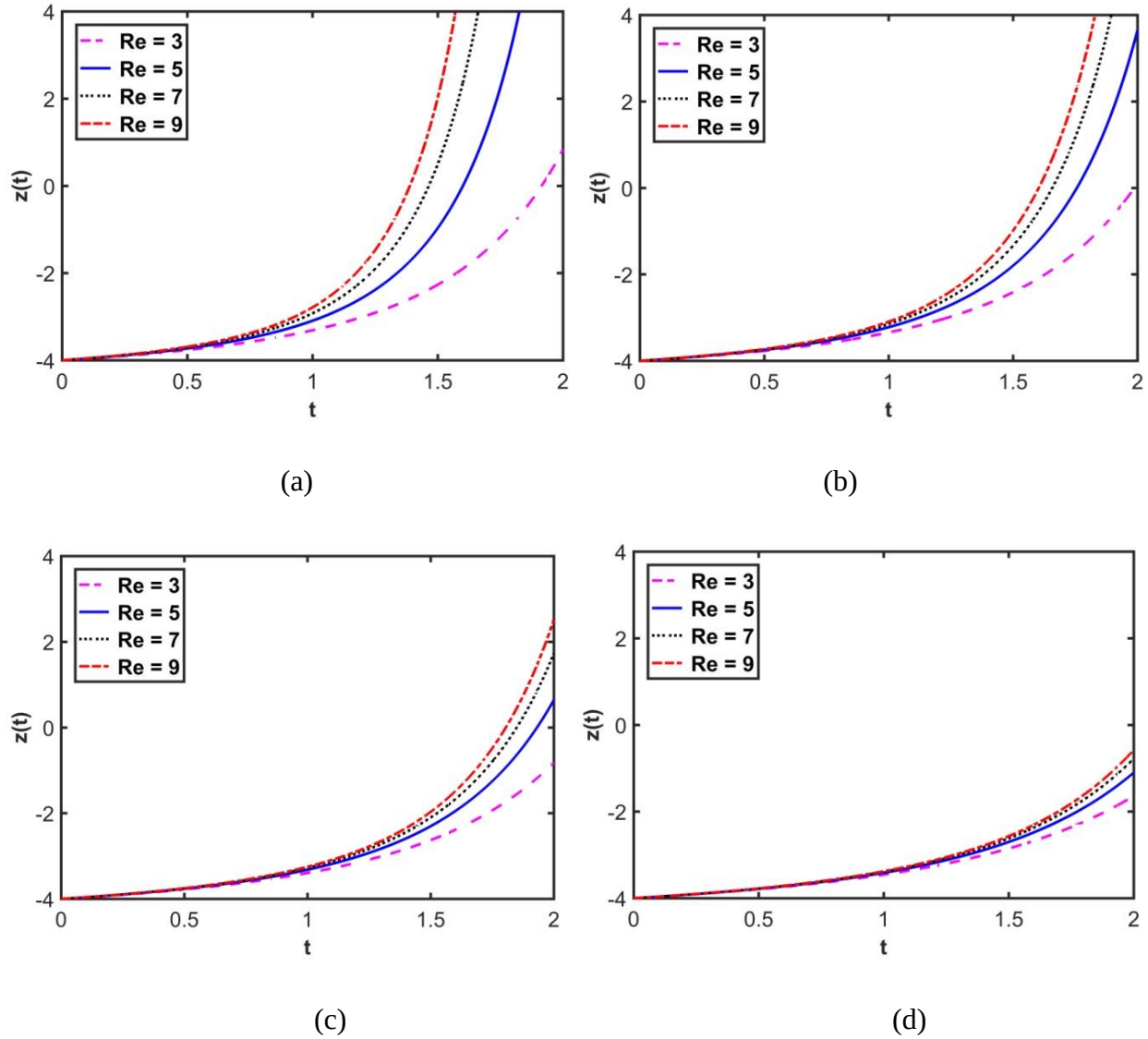


Figure 5.10 Axial trajectories of carrier particles profile for different Re when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1$.

5.9.5. Effect of Pulsatile frequency

The blood pumped by the heart in the artery produces the pulsatile behavior of blood flow and results in pulsatile frequency (the frequency of oscillation) ω . The pulsatile frequency is involved

in the pressure gradient and proportionally impacts on the pressure gradient. In this study, we have considered the values of ω as 1, 4, 7, and 10. In physical terms, the pressure gradient decreases with a decrease in pulsatile frequency, which essentially decreases the fluid velocity along the axis of the microvessel. As a result, a higher value of pulsatile frequency ω supported the drug carrier particles to travel far from the arterial wall (tumor position) as shown in figure 5.12. However, an opposite trend is demonstrated in the case of axial trajectories of carrier particles (Fig. 5.13) and total volume fraction of magnetic nanoparticles (Fig. 5.14).

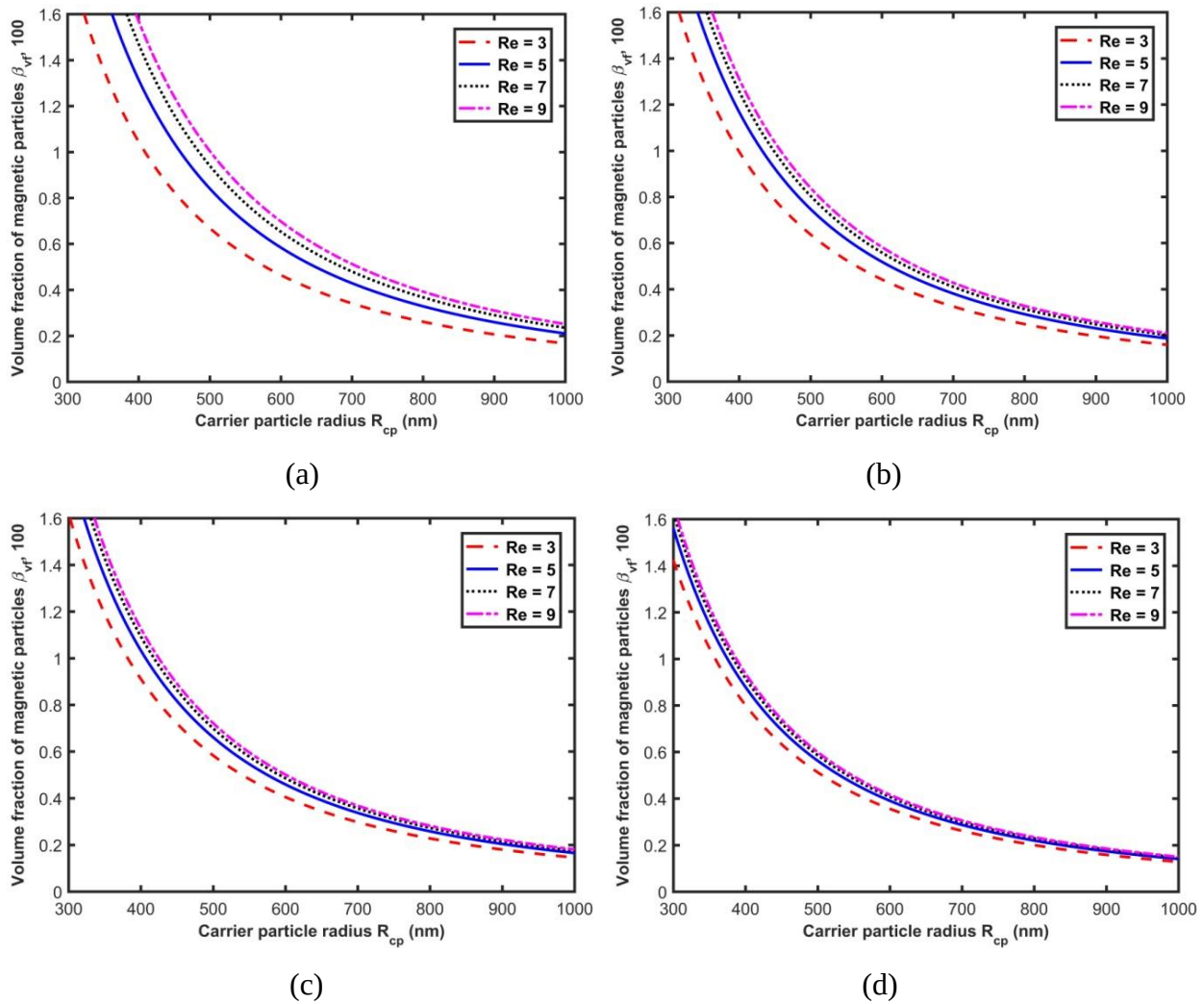


Figure 5.11 Profile of total volume fraction ($\beta_{vf,100}$) vs. R_{cp} for various Re when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1$.

5.9.6. Effect of tumor-magnet distance

The effect of tumor-magnet distance on the total volume fraction of magnetic nanoparticles is shown in Fig. 5.15. In the current work to calculate $\beta_{vf,100}$ as a function of R_{cp} , four different magnet-blood vessel distances $d = 0.03, 0.04, 0.05$, and $0.06m$ are considered. We observe from the figure that magnet-blood vessel distance supports the capture efficiency of the drug carrier particles as $\beta_{vf,100}$ moves towards lower value and it further supports larger drug carrier particles.

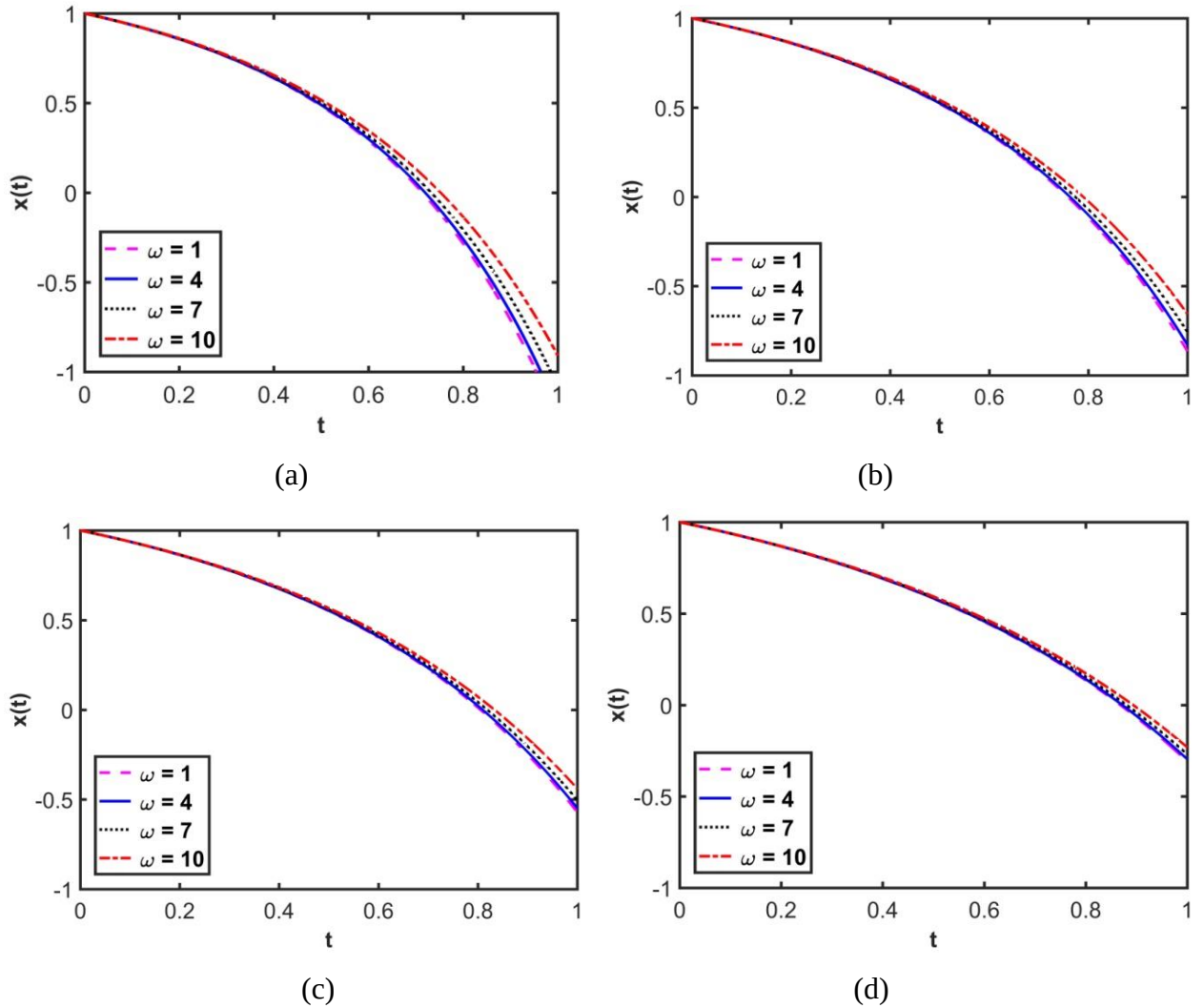


Figure 5.12 Radial trajectories of carrier particles profile for different ω when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1$.

5.9.7. Impact of blood rheology

The rheology of the blood is considered with the Casson fluid nature, and it is involved in the form of Casson parameter. The effect of the Casson parameter on the total volume fraction of magnetic nanoparticles is demonstrated in Fig. 5.16. From the figure it is shown that capture efficiency of carrier particles boosts up with enhancement in Casson parameter. Hence carrier particles radius and volume fraction needed for capture efficiency boost up with increase in Casson parameter. Improved Casson parameter leads to the Newtonian nature of the blood. Hence, the non-Newtonian rheology needs larger carrier particles to be captured at the specific region than the Newtonian fluid.

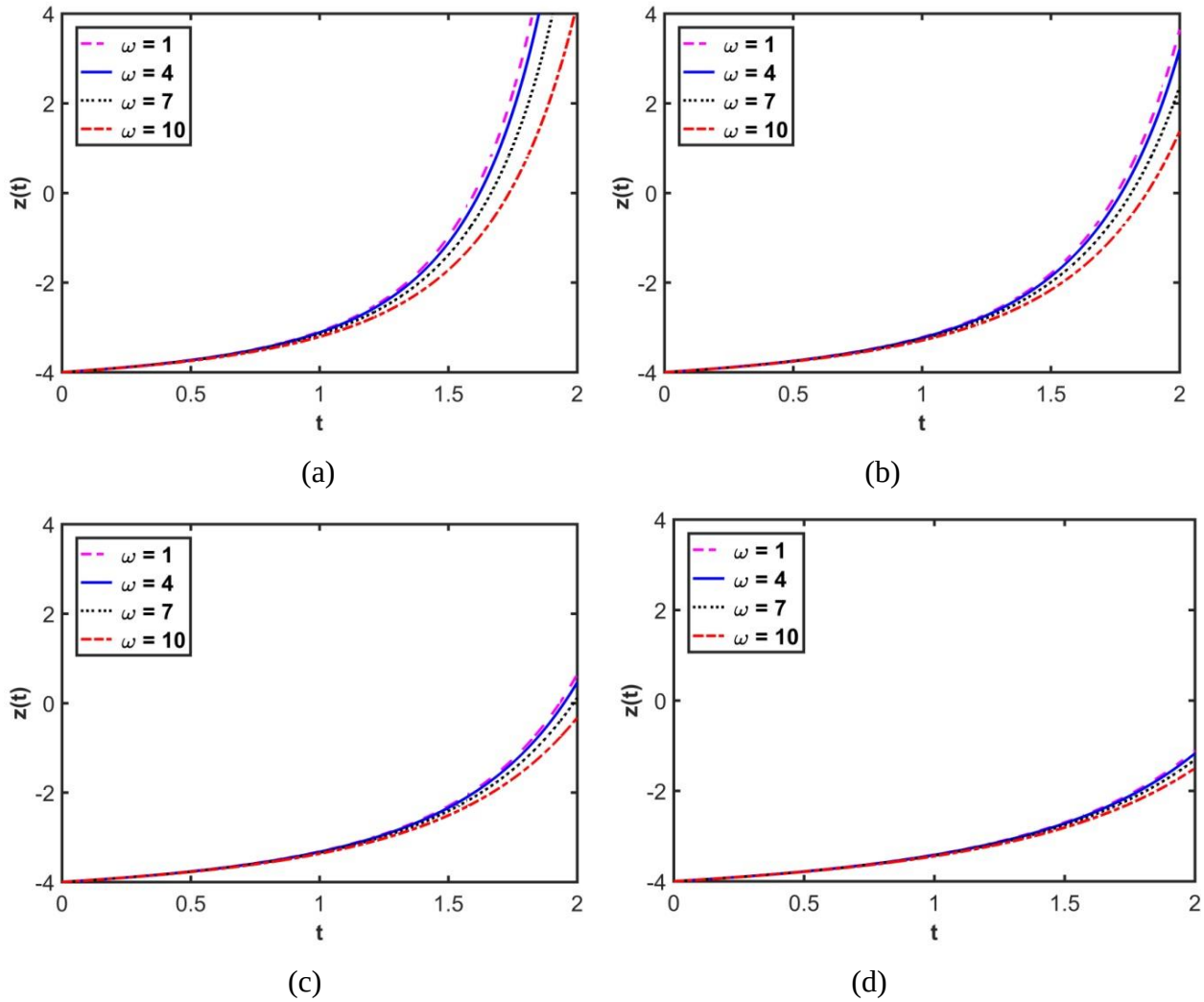


Figure 5.13 Axial trajectories of carrier particles profile for different ω when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1$.

5.9.8. Effect of hematocrit

Fig. 5.17 depicts the influence of hematocrit parameters on the total volume fraction of magnetic nanoparticles. Hematocrit is the percentage of RBCs in the blood, and it plays an indispensable role in the capture capacity of carrier particles. The capture efficiency of carrier particles observed boost up with decrease in Hematocrit parameter. However, higher hematocrit leads to a coronary insufficiency and myocardial infarction [208]. Hence, the efficiency of curing diseases faced difficulty during the treatment of cardiovascular disorders due to higher hematocrit.

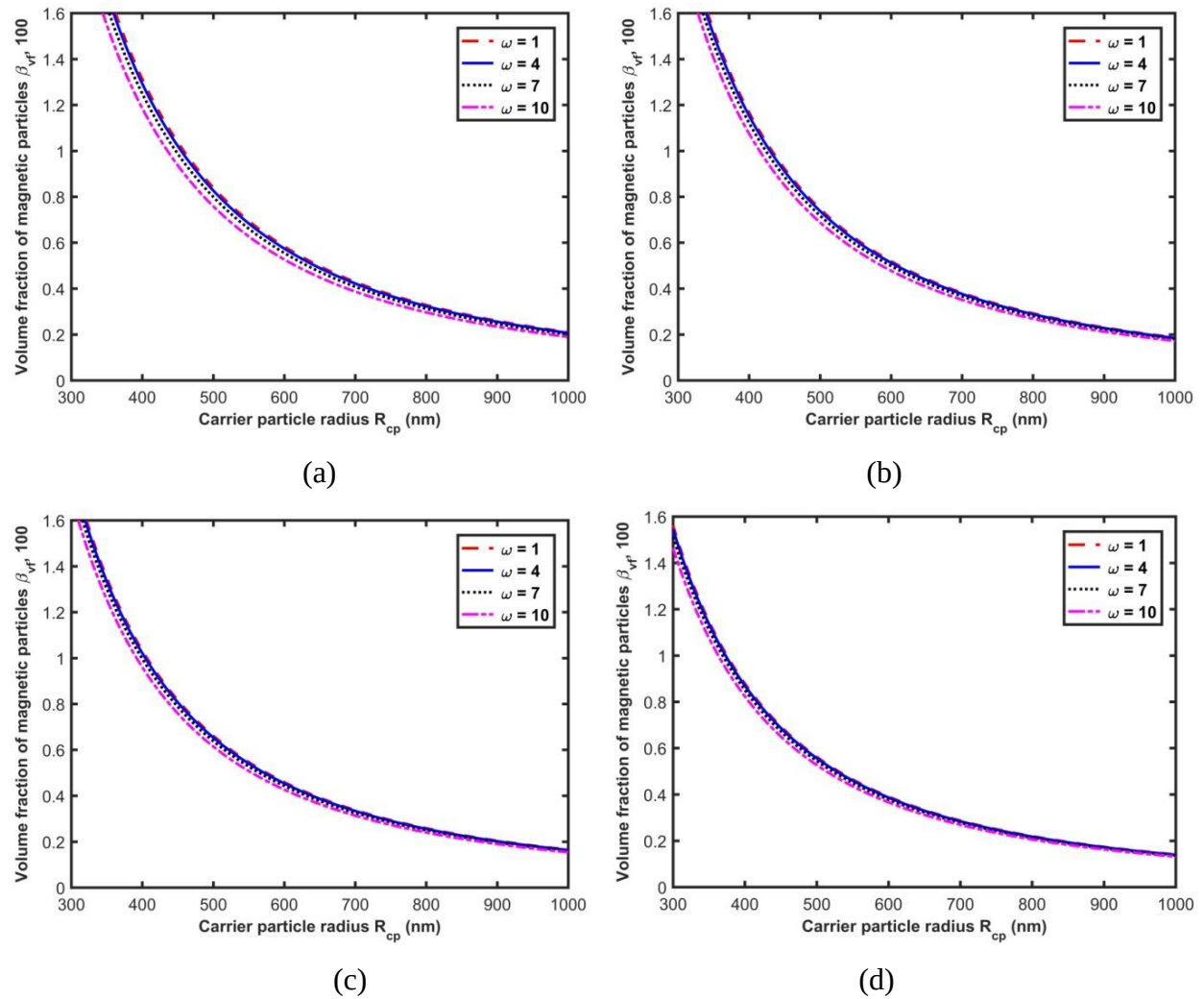


Figure 5.14 Profile of total volume fraction ($\beta_{vf,100}$) vs. R_{cp} for various ω when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1$.

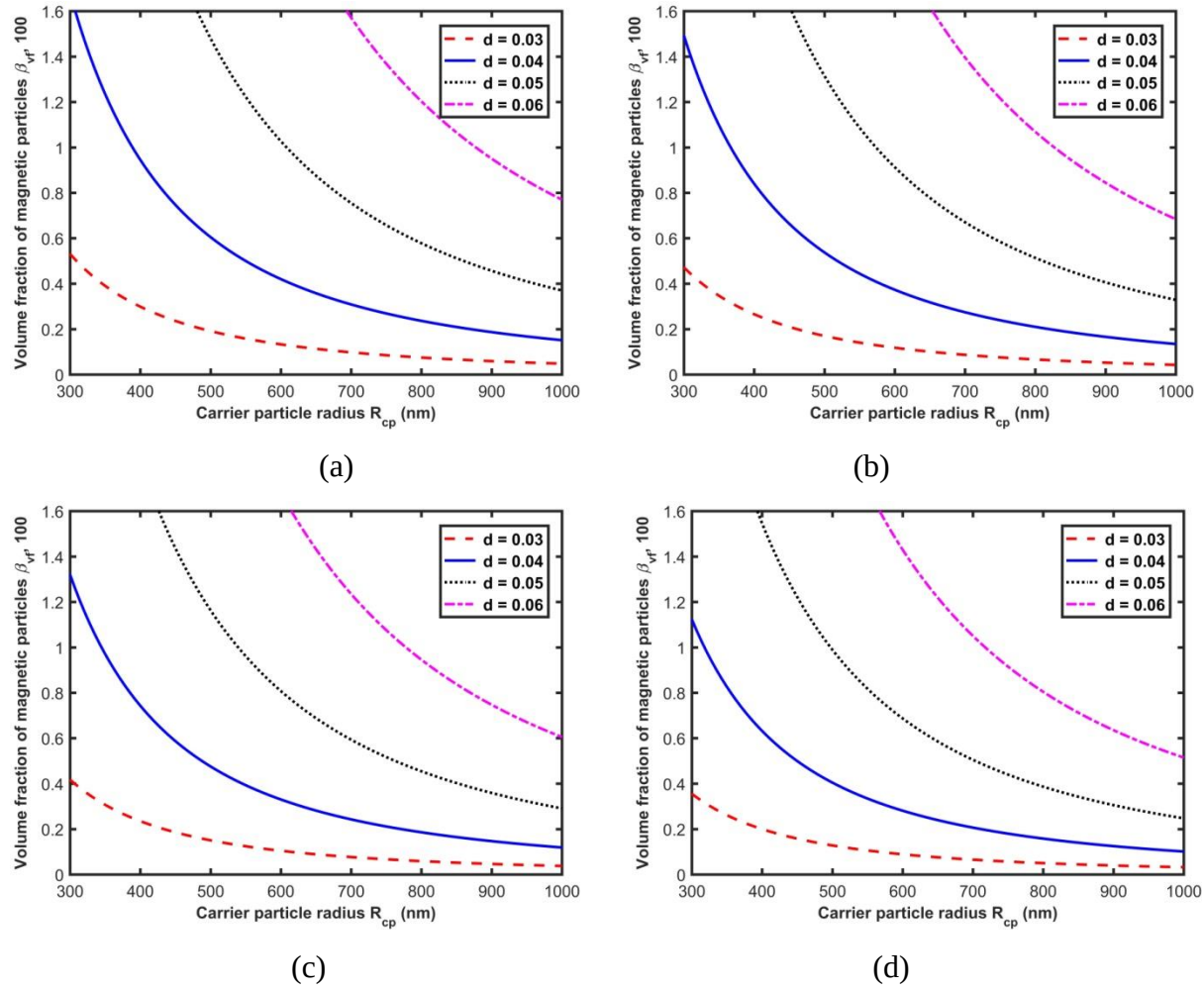


Figure 5.15 Profile of total volume fraction ($\beta_{vf,100}$) vs. R_{cp} for various d when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1$.

5.9.9. Conclusion

The purpose of the present study is to investigate the projection of the trajectories of drug carrier particles at tumor position in a microvessel of Casson blood flow during magnetic drug targeting. The time-fractional Caputo derivative is introduced in the governing equation. Analytic solution for the average fluid velocity is determined from the momentum equation using integral transforms (Laplace transform, and finite Hankel transform of order zero). Total volume fraction of magnetic nanoparticles is solved analytically. Fractional order parameter time memory effects on trajectories of carrier particles and total volume fraction of nanoparticles have been discussed. The effects of biophysical parameters such as magnetization, Darcy number, Reynolds number, pulsatile

frequency, tumor – magnet distance, Casson, and Hematocrit parameter on the capture capacity of carrier particles with different values of fractional parameter have been discussed.

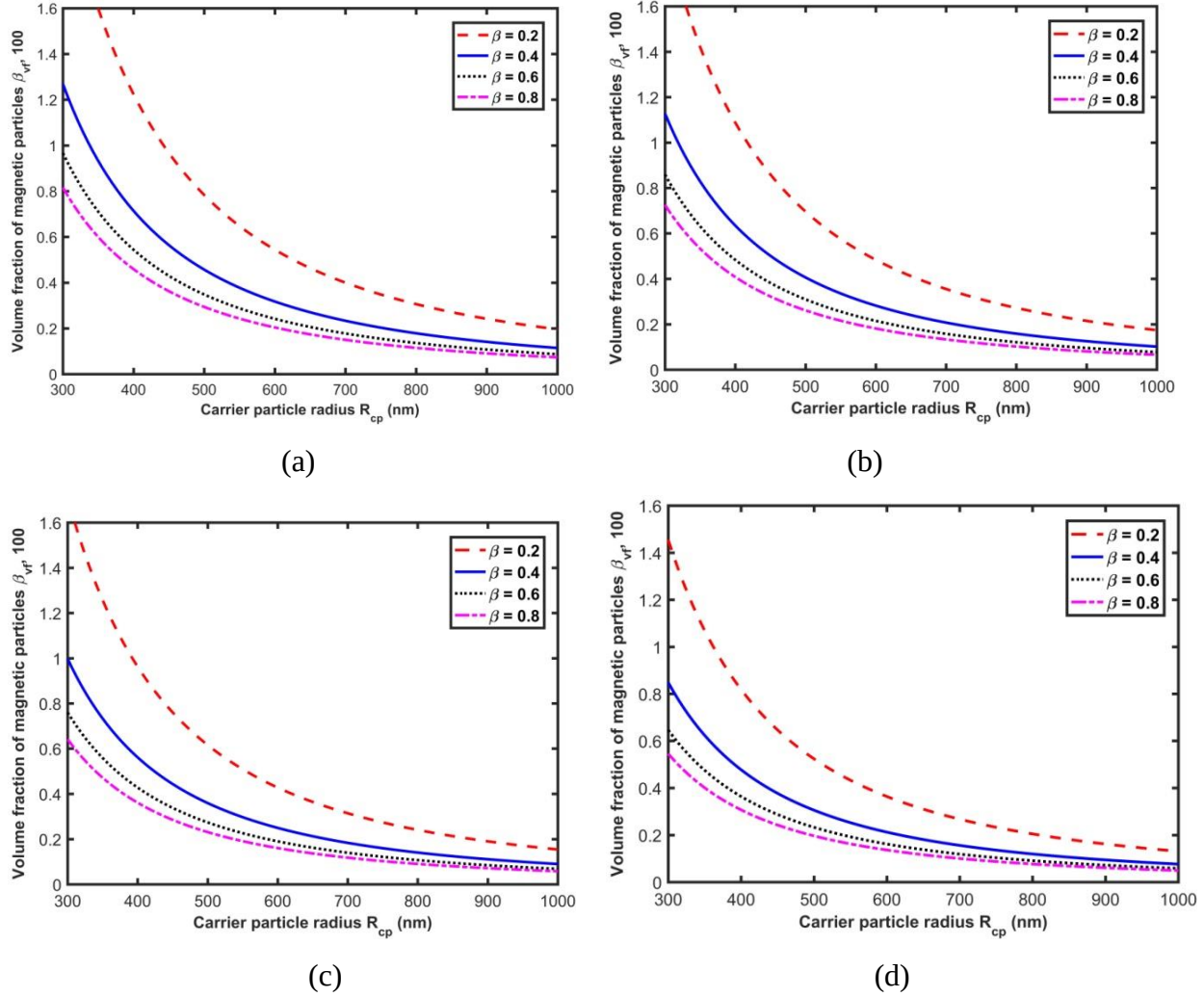


Figure 5.16 Profile of total volume fraction ($\beta_{vf,100}$) vs. R_{cp} for various β when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1$.

Moreover, from the present study, the following important outcomes can be drawn:

- The fractional order parameter enhances the radial movement of carrier particles while it restricts axial movement of carrier particles.
- The radial projection of trajectories of carrier particles boosts up with enhancement in magnetization, Darcy number, and Reynolds number, whereas it restricts the axial trajectories.

- A decrease in pulsatile frequency increases the radial trajectory of carrier particles to tumor site, whereas it limits the axial trajectories.
- The total volume fraction of magnetic nanoparticles decreases with enhancement in magnetization parameters.
- A decrease in Darcy number, Reynolds number, and tumor magnet distance decreases the total volume fraction of nanoparticles.
- Total volume fraction of magnetic nanoparticles decreases with increase in pulsatile frequency, Casson parameter and Hematocrit parameter.

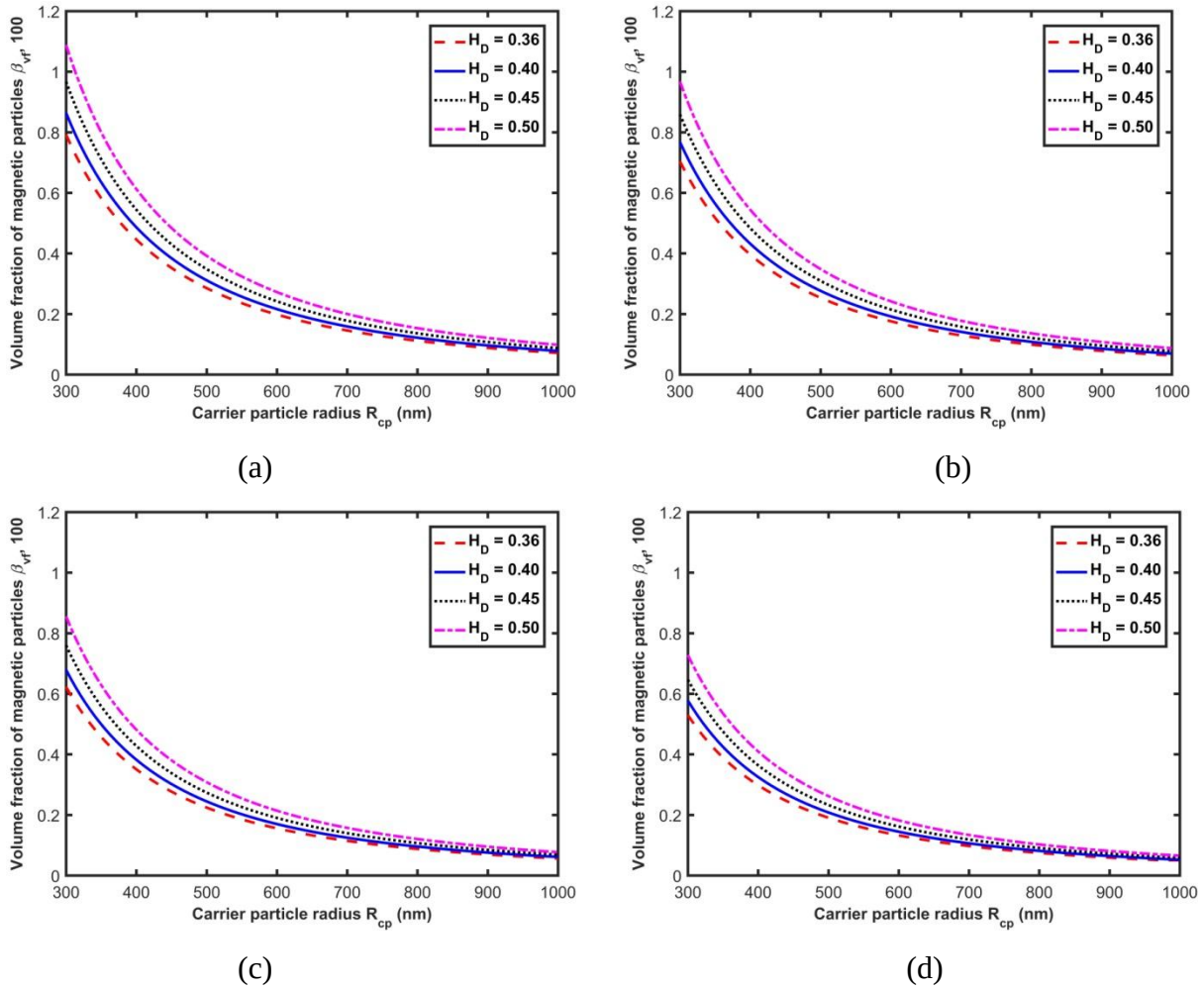


Figure 5.17 Profile of total volume fraction ($\beta_{vf,100}$) vs. R_{cp} for various H_D when (a) $\alpha = 0.6$ (b) $\alpha = 0.8$ (c) $\alpha = 0.9$ (d) $\alpha = 1$.

Moreover, the findings of the present study can be helpful to determine capture efficiency of the drug carrier at the tumor region under certain circumstances. Furthermore, the outcomes of this study will be used to provide opportunities to develop apparatus and medical devices related to non-invasive controlled drug targeting during magnetic drug targeting.

6. Analysis of unsteady non-Newtonian Jeffrey blood flow and transport of magnetic nanoparticles through an inclined porous artery with stenosis using the time fractional derivative[‡]

6.1. Introduction

The transport of hormones, oxygen, and nutrients to cells is carried out by the cardiovascular system. The cardiovascular system takes waste products produced by metabolic activities and delivers them to other organs for disposal. The cardiovascular system plays a crucial role in circulating blood flow in the body. However, the thickening or hardening of the arteries, known as atherosclerosis, affects the cardiovascular system. The main cause of atherosclerosis is the accumulation of fatty substances in the internal lining of the vessel, which prevents blood from flowing freely. This kind of disorder is commonly known as stenosis. According to the World Health Organization (WHO), cardiovascular diseases cause 17.6 million deaths each year, an estimated 32% of all deaths worldwide [209]. The restriction of blood flow caused by stenosis affects the normal functioning of the cardiovascular system, generally leading to cardiovascular disorders. In the past few decades, practical interest in the characterization of blood flow through stenotic arteries has received the attention of many researchers. For example, Akbar et al. [210] studied the flow of nanofluid through a permeable composite stenosis artery by using the homotopy perturbation technique. Xingting et al. [211] demonstrated the thermal condition of blood flow through an artery with multiple stenosis and angles by employing the finite volume method. Zaman et al. [212] analyzed nanoparticles transport during blood flow in the affected artery due to the combined impacts of stenosis and aneurysm. In the above studies and studies carried out by researchers in Refs. [213 – 217], showed the axial direction of blood flow is taken in the horizontal direction. However, in some circumstances, blood vessels can make an angle of inclination horizontally. Accordingly, several researchers formulated blood flow models and

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demonstrated the impacts caused by (chemical reactions, slip velocity, and heat source [218], overlapping stenosis and dilatation [219], body acceleration and slip velocity [220], and Hall currents [221]) on blood flow through an inclined stenosis artery.

Recently, different procedures of therapy have been used to avoid atherosclerosis in the artery, for instance, by using percutaneous transluminal coronary angioplasty and atherectomy. However, after the application of these therapies, the emergence of restenosis in the blood vessel can occur again [222]. On the other hand, traditional drug delivery systems like anti-thrombotic and anti-proliferative drugs are incapable of accumulating enough drugs at the target region and can cause side effects in non-target regions due to the nature of free drugs [223]. To overcome these drawbacks, magnetic drug targeting (MDT) could be suggested. Magnetic drug targeting with the help of magnetic nanoparticles (MNPs) to treat cardiovascular disorders under the application of an external magnetic field is an imperative area of study. During the past decades, research interest in magnetic drug targeting has increased significantly because of its compatibility, noninvasive nature, and high targeting efficiency as compared to traditional drug delivery systems [156, 224, 225]. Efficient targeted drug delivery plays an important role in the medication of many diseases, and among them is a cardiovascular disorder caused by defects such as stenosis and thrombosis [226]. Alishiri et al. [227] suggested magnetic drug targeting for increasing the transport of drug carriers to the atherosclerosis disease in the artery. Nanoparticles play a vital role in delivering drugs to diseased tissue. In addition, the development of nanotechnology contributes a lot to the medical world by detecting and diagnosing diseases, such as cancer and atherosclerosis, at their early stages [228].

A fluid that does not obey the linear correlation between shear stress and rate of strain is known as a non-Newtonian fluid (NNF). Non-Newtonian fluids (NNFs) have become an interesting area of study because of their abundant applications in medical science, bioengineering, and industries. Some examples are oil, blood at low shear rates in small vessels, toothpaste, gels, drilling mud, and so on. Due to their complex nature, non-Newtonian fluids are categorized into three types of governing equations: rate, differential, and integral. Among the non-Newtonian fluids, the one that is described in relation to the relaxation and retardation time parameters is Jeffrey fluid. Jeffrey fluid is a rate-type non-Newtonian fluid that can be analyzed in terms of the impacts of the ratio between relaxation and retardation times, and the retardation time parameters [229 - 232]. One important characteristic of the Jeffrey fluid model is that it can be reduced to other fluid models

with the appropriate selection of Jeffrey fluid parameters. Having this in mind, various researchers presented the behavior of Jeffrey fluid flow of blood through stenosis arteries subject to the impacts of various physical parameters [233 – 236]. The study of fluid flow in porous vessels has gained considerable interest from researchers due to its various practical applications. The flow in porous media has various engineering applications, for instance, blood flow in capillaries, dialysis in artificial kidneys, engine coolant systems, aircraft wings, the design of filters, and many others [237, 238]. Excellent findings on flow in porous media can be found in refs. [239 – 242].

Fractional mathematical models containing time derivatives play an imperative role in the study of fluid flow. Recently, mathematical models of fluid flow involving time fractional derivatives have inspired the interest of various researchers due to the impact of time memory on the outcome solution. The time fractional derivative model contains more information than the classical derivative model of the same kind. Anwar et al. [243] presented the Caputo-Fabrizio (C-F) time fractional derivative model and analyzed the influences of ramped velocity, Newtonian heating, radiation, and magnetohydrodynamics (MHD) on Jeffrey fluid flow. Imran et al. [244] demonstrated the impacts of radiation and chemical reactions on magnetohydrodynamics Jeffrey fluid flow using the C-F time fractional derivative model without a singular kernel. Ali et al. [245] demonstrated a comparative study on a generalized Jeffrey nanofluid employing C-F and Atangana-Baleanu fractional order derivative models. Other findings on fractional Jeffrey fluid models exist in references [246, 247].

The afore mentioned literature surveys show the intensive analysis of Jeffrey fluid flow using the C-F fractional derivative. Jeffrey nanofluid flow has also been discussed by a few researchers. However, the analysis of magnetic nanoparticle transport for drug delivery applications through inclined porous arteries with mild stenosis by treating blood as a non-Newtonian Jeffrey fluid model theoretically in the C-F fractional sense has not been explored yet. As a result, the aim of the present analysis is to fill this gap. The novelty of the present problem involves the following:

- The non-Newtonian visco-elastic Jeffrey fluid represents the rheology of blood.
- The C-F time-fractional derivative model is used to impose the memory effect.
- The blood flow and transport of magnetic nanoparticles take place through an inclined artery with stenosis.

- In the presence of a magnetic field, magnetic nanoparticles are used in drug delivery applications.

First, the geometry of mild stenosis along with the governing equations of blood flow and transport of magnetic nanoparticles are presented. These equations are transformed into dimensionless forms using dimensionless parameters. The dimensionless governing equations are converted into a C-F time-fractional derivative model [103]. Secondly, the analytic solutions for the velocities of blood and magnetic nanoparticles are obtained using Laplace transform and finite Hankel transform of order zero along with their inverses, and the solutions are written in the form of Laplace convolutions. Finally, using the MATLAB software, the numerical results are plotted for illustration. The study presents the effects of various parameters such as fractional parameter, Darcy number, Jeffrey fluid parameter, stenosis height, inclination angle, Hartmann number, shape parameter, and magnetic nanoparticles concentration parameter in the stenosis region. The outcomes of the present study will give insight into understanding the transport of magnetic nanoparticles during magnetic drug targeting and the dynamics of blood flow due to the presence of atherosclerosis.

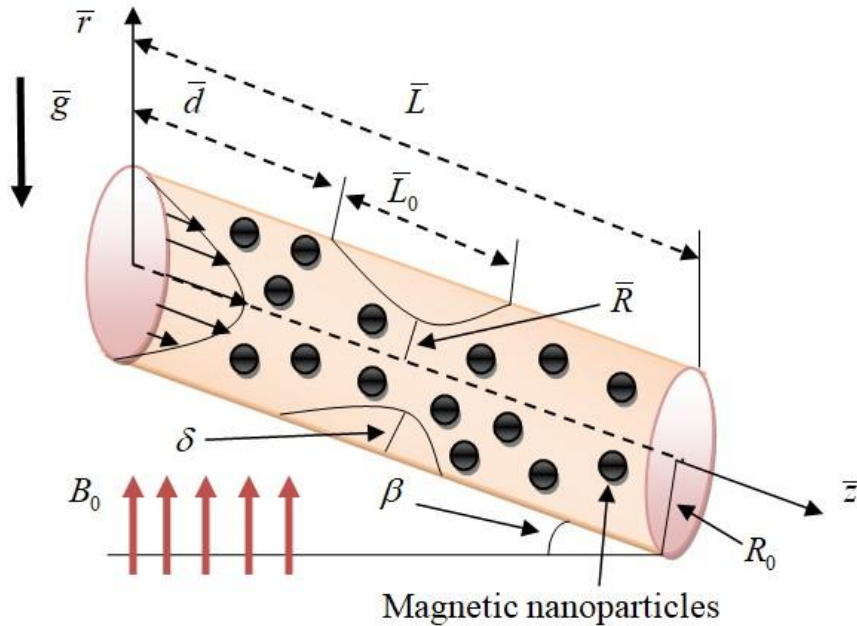


Figure 6.1 Geometrical model of the problem.

6.2. Problem formulation

In the present study, unsteady incompressible non-Newtonian Jeffrey fluid flow of blood along with magnetic nanoparticles through an inclined artery with mild stenosis is considered (Fig. 6-1). It is assumed that the flow field is unidirectional and that the magnetic nanoparticles are distributed uniformly throughout the blood. Here, the vertical axis (r -axis) is the radial axis, and the artery which makes an angle β with the horizontal, is taken along the z -axis while the uniform magnetic field is applied in the vertical direction. At time $\bar{t} = 0$, there is no motion in the system. Maxwell's equations describe magnetic field strength, while Newton's second law of motion demonstrates the transport of magnetic nanoparticles. The momentum equation describes the flow of blood along the flow axis.

The electromagnetic force is governed by Maxwell's relations [129, 248]

$$\begin{aligned}\nabla \times \vec{B} &= \mu_0 \vec{J}, \\ \nabla \cdot \vec{B} &= 0, \\ \nabla \times \vec{E} &= -\frac{\partial \vec{B}}{\partial t}.\end{aligned}\tag{6.1}$$

where, μ_0 , $\vec{E}$ and $\vec{J}$ are the magnetic permeability, electric field intensity and the current density, respectively. $\vec{B} = \vec{B}_0 + \vec{b}_0$ is magnetic flux intensity, B_0 is the applied magnetic field strength in the radial direction and $\vec{b}_0$ is the induced magnetic field. $\vec{J}$ can be given by

$$\vec{J} = \sigma (\vec{E} + \vec{V} \times \vec{B}).\tag{6.2}$$

The induced magnetic field $\vec{b}_0$ is negligible due to a very small Reynolds number. Moreover, it is considered that there is no applied voltage and polarization in the system, as the result the electric field $\vec{E}$ is disregarded. Having these assumptions, we define the electromagnetic force $\vec{F}_m$ by

$$\vec{F}_m = \vec{J} \times \vec{B} = \sigma (\vec{V} \times \vec{B}) \times \vec{B} = -\sigma B_0^2 u(r, t) \vec{k},\tag{6.3}$$

where σ , $\vec{V} = u(r, t)\vec{k}$, and $\vec{k}$ are the electrical conductivity, velocity field, the standard unit vector in the z – direction, respectively.

The equation that describes radially non-symmetric and axially symmetric stenosis is [249, 250]

$$\bar{R}(\bar{z}) = \begin{cases} R_0 + R_0 \bar{Y} \left[(\bar{z} - \bar{d})^w - \bar{L}_0^{(w-1)} (\bar{z} - \bar{d}) \right], & \bar{d} < \bar{z} < \bar{d} + \bar{L}_0, \\ R_0, & \text{elsewhere,} \end{cases} \quad (6.4)$$

where, $\bar{Y} = \frac{\bar{\delta} w^{(w/(w-1))}}{R_0 \bar{L}_0^w (w-1)}$, $\bar{R}(\bar{z})$ is the radius of the stenosis, and R_0 is the radius of the vessel, $\bar{d}$ is the location of the stenosis and $\bar{L}_0$ is its length, $w \geq 2$ is the stenosis shape parameter (where $w=2$ denote the symmetric stenosis), and $\bar{\delta}$ is the maximum height of the stenosis at $\bar{Z} = \bar{d} + \frac{\bar{L}_0}{w^{(1/(w-1))}}$ with $\bar{\delta} < R_0$.

The unsteady Jeffrey fluid flow of blood in cylindrical polar coordinates $(\bar{r}, \bar{\theta}, \bar{z})$ is governed by the momentum equation [251 – 253].

$$\begin{aligned} \frac{\partial}{\partial \bar{t}} (\bar{u}(\bar{r}, \bar{t})) - \frac{1}{\rho} \frac{\partial \bar{p}}{\partial \bar{z}} &= \frac{1}{\rho} \frac{1}{\bar{r}} \frac{\partial}{\partial \bar{r}} (\bar{r} \bar{S}_{\bar{r}\bar{z}}) + \frac{K_s N}{\rho} (\bar{v}(\bar{r}, \bar{t}) - \bar{u}(\bar{r}, \bar{t})) - \frac{\mu}{k_p \rho} \bar{u}(\bar{r}, \bar{t}) \\ &+ \bar{\Psi}(\bar{t}) - \frac{\sigma B_0^2 \sin \beta}{\rho} \bar{u}(\bar{r}, \bar{t}) + \bar{g} \sin \beta, \end{aligned} \quad (6.5)$$

where the extra tensor of the Jeffrey fluid $\bar{S}_{\bar{r}\bar{z}}$ is of the form

$$\bar{S}_{\bar{r}\bar{z}} = \mu \left(\frac{1}{1 + \lambda_1} \right) \left[1 + \lambda_2 \left(\bar{u}_{\bar{r}}(\bar{r}, \bar{t}) \frac{\partial}{\partial \bar{r}} + \bar{u}(\bar{r}, \bar{t}) \frac{\partial}{\partial \bar{z}} \right) \right] \left(\frac{\partial}{\partial \bar{z}} (\bar{u}_{\bar{r}}(\bar{r}, \bar{t})) + \frac{\partial}{\partial \bar{r}} (\bar{u}(\bar{r}, \bar{t})) \right). \quad (6.6)$$

The velocities $\bar{u}_{\bar{r}}(\bar{r}, \bar{t})$, $\bar{u}(\bar{r}, \bar{t})$, and $\bar{v}(\bar{r}, \bar{t})$ are the radial and axial velocities of blood, and velocity of magnetic nanoparticles, respectively. The constants ρ , μ , K_s , and k_p are the density of blood, dynamic viscosity of blood, the Stoke's constant, and the permeability of the porous medium, respectively. N represents the number of magnetic nanoparticles per unit volume,

$\frac{K_s N}{\rho}(\bar{v}(\bar{r}, \bar{t}) - \bar{u}(\bar{r}, \bar{t}))$ describes the force between magnetic nanoparticles and blood that

happens due to their relative motion, $\bar{g}$ is the acceleration due to gravity, λ_1 is the ratio between relaxation and retardation times, λ_2 is the retardation time.

Taking into account the unidirectional flow and substitution of Eq. (6.6) into Eq. (6.5) yields

$$\begin{aligned} \frac{\partial}{\partial \bar{t}}(\bar{u}(\bar{r}, \bar{t})) = & -\frac{1}{\rho} \frac{\partial \bar{p}}{\partial \bar{z}} + \frac{\nu}{1 + \lambda_1} \left(\frac{\partial^2}{\partial \bar{r}^2} + \frac{1}{\bar{r}} \frac{\partial}{\partial \bar{r}} \right) \bar{u}(\bar{r}, \bar{t}) + \frac{K_s N}{\rho} (\bar{v}(\bar{r}, \bar{t}) - \bar{u}(\bar{r}, \bar{t})) \\ & - \frac{\mu}{k_p \rho} \bar{u}(\bar{r}, \bar{t}) + \bar{\Psi}(\bar{t}) - \frac{\sigma B_0^2 \sin \beta}{\rho} \bar{u}(\bar{r}, \bar{t}) + \bar{g} \sin \beta, \end{aligned} \quad (6.7)$$

where ν is the kinematic viscosity.

The transport of magnetic nanoparticles is described in accordance with Newton's 2nd law of motion, which is given by

$$M_m \frac{\partial}{\partial \bar{t}}(\bar{v}(\bar{r}, \bar{t})) = K_s (\bar{u}(\bar{r}, \bar{t}) - \bar{v}(\bar{r}, \bar{t})), \quad (6.8)$$

where M_m represents average mass of magnetic nanoparticles.

The oscillating pressure gradient of blood flow in Eq. (6.7) has the form [144, 254, 255]

$$-\frac{\partial \bar{p}}{\partial \bar{z}} = \bar{q}_0 + \bar{q}_1 \cos(\bar{\varphi} \bar{t}), \quad \bar{t} > 0, \quad (6.9)$$

where $\bar{q}_0$, $\bar{q}_1$ and $\bar{\varphi}$ represents the steady amplitude, amplitude of the transient part and the frequency of pulsation, respectively.

The periodic body acceleration $\bar{\Psi}(\bar{t})$ in Eq. (6.7) is given by [256, 257]

$$\bar{\Psi}(\bar{t}) = \bar{\ell}_0 \cos(\bar{k} \bar{t} + \gamma_0), \quad (6.10)$$

where $\bar{\ell}_0$, γ_0 and $\bar{k}$ are the amplitude, the difference with the pulsatile pressure gradient, and the body acceleration frequency, respectively.

To introduce the C-F time fractional derivative to Eqs. (6.7) and (6.8) we multiply the equations

by $\Lambda = \sqrt{\frac{R_0 \rho}{q_0}}$ [200] (with unit of time) which yields

$$\begin{aligned} \Lambda^\alpha D_t^\alpha \bar{u}(\bar{r}, \bar{t}) &= \frac{\Lambda}{\rho} (\bar{q}_0 + \bar{q}_1 \cos(\bar{\varphi} \bar{t})) + \frac{\Lambda \nu}{1 + \lambda_1} \left(\frac{\partial^2}{\partial \bar{r}^2} + \frac{1}{\bar{r}} \frac{\partial}{\partial \bar{r}} \right) \bar{u}(\bar{r}, \bar{t}) \\ &+ \frac{\Lambda K_s N}{\rho} (\bar{v}(\bar{r}, \bar{t}) - \bar{u}(\bar{r}, \bar{t})) - \frac{\Lambda \mu}{k_p \rho} \bar{u}(\bar{r}, \bar{t}) + \Lambda \bar{\ell}_0 \cos(\bar{k} \bar{t} + \gamma_0) \\ &- \frac{\Lambda \sigma B_0^2 \sin \beta}{\rho} \bar{u}(\bar{r}, \bar{t}) + \Lambda \bar{g} \sin \beta, \end{aligned} \quad (6.11)$$

$$M_m \Lambda^\alpha D_t^\alpha \bar{v}(\bar{r}, \bar{t}) = \Lambda K_s (\bar{u}(\bar{r}, \bar{t}) - \bar{v}(\bar{r}, \bar{t})), \quad (6.12)$$

where, the C-F time fractional derivative model is given by [103]

$${}^{C-F} D_t^\alpha u(r, t) = \frac{1}{1 - \alpha} \int_0^t \exp\left[\frac{-\alpha(t - \tau)}{1 - \alpha}\right] u'(r, \tau) d\tau, \quad 0 < \alpha < 1. \quad (6.13)$$

The Laplace transform of Eq. (6.13) can have the form

$$L[{}^{C-F} D_t^\alpha u(r, t)] = \frac{sL[u(r, t)] - u(r, 0)}{s + (1 - \alpha)\alpha}. \quad (6.14)$$

Eqs. (6.7) and (6.8) are subject to the following initial conditions (ICs) and boundary conditions (BCs)

$$\begin{aligned} \bar{u}(\bar{r}, 0) &= 0, \bar{v}(\bar{r}, 0) = 0, \text{ for } \bar{t} = 0 \text{ and } \bar{r} \in [0, \bar{R}], \\ \bar{u}(\bar{r}, \bar{t}) &= 0, \bar{v}(\bar{r}, \bar{t}) = 0, \text{ for } \bar{t} > 0 \text{ and } \bar{r} = \bar{R}, \end{aligned} \quad (6.15)$$

where, $\bar{R} = \bar{R}(\bar{z})$.

For dimensionless study, we use the following dimensionless parameters [126]

$$\left. \begin{aligned} r = \frac{\bar{r}}{R_0}, t = \frac{\bar{t}}{\Lambda}, u = \frac{\Lambda \bar{u}}{R_0}, v = \frac{\Lambda \bar{v}}{R_0}, g = \frac{\Lambda^2 \bar{g}}{R_0}, q_0 = \frac{\Lambda^2 \bar{q}_0}{\rho R_0}, q_1 = \frac{\Lambda^2 \bar{q}_1}{\rho R_0}, \varphi = \Lambda \bar{\varphi}, \\ k = \Lambda \bar{k}, \ell_0 = \frac{\Lambda^2 \bar{\ell}_0}{R_0}, z = \frac{\bar{z}}{R_0}, d = \frac{\bar{d}}{R_0}, L_0 = \frac{\bar{L}_0}{R_0}, R = \frac{\bar{R}}{R_0}, \delta = \frac{\bar{\delta}}{R_0}. \end{aligned} \right\} \quad (6.16)$$

Upon using Eq. (6.16) into Eqs. (6.11) and (6.12), yields

$$\begin{aligned} D_t^\alpha u(r, t) = q_0 + q_1 \cos(\varphi t) + \frac{1}{\text{Re}(1 + \lambda_1)} \left(\frac{\partial^2}{\partial r^2} + \frac{1}{r} \frac{\partial}{\partial r} \right) u(r, t) + \frac{pc}{\text{Re}} (v(r, t) - u(r, t)) \\ - \frac{1}{\text{Da Re}} u(r, t) + \ell_0 \cos(kt + \gamma_0) - \text{Ha}^2 u(r, t) + g \sin \beta, \end{aligned} \quad (6.17)$$

$$p_m D_t^\alpha v(r, t) = u(r, t) - v(r, t), \quad (6.18)$$

where $\text{Re} = \frac{R_0^2}{\Lambda \nu}$ is the Reynolds number, $pc = \frac{K_s N R_0^2}{\mu}$ is the particle concentration parameter,

$\text{Da} = \frac{k_p}{R_0^2}$ is the Darcy number, $\text{Ha} = B_0 \sqrt{\sigma} \sqrt{\frac{R_0}{\rho}} \sin \beta$ is the Hartman number, and $p_m = \frac{M_m}{K_s \Lambda}$

is the mass parameter of particles.

The corresponding dimensionless ICs and BCs to Eqs. (6.17) and (6.18) are

$$\begin{aligned} u\left(\frac{r}{R}, 0\right) = 0, v\left(\frac{r}{R}, 0\right) = 0, \text{ for } t = 0 \text{ and } \frac{r}{R} \in [0, 1], \\ u(1, t) = 0, v(1, t) = 0, \text{ for } t > 0 \text{ and } \frac{r}{R} = 1. \end{aligned} \quad (6.19)$$

The stenosis equation in dimensionless form can be written as

$$R(z) = \begin{cases} 1 + \Upsilon \left[(z - d)^w - L_0^{w-1} (z - d) \right], & d < z < d + L_0, \\ 1, & \text{elsewhere,} \end{cases} \quad (6.20)$$

with $\Upsilon = \frac{\delta w^{(w/(w-1))}}{L_0^w (w-1)}$, $z = d + \frac{L_0}{w^{(1/(w-1))}}$, and $\delta < 1$.

Introducing the dimensionless radial transformation coordinate $y = \frac{r}{R}$, Eq. (6.19) takes the form

$$\begin{aligned} u(y, 0) = 0, v(y, 0) = 0, \text{ for } t = 0 \text{ and } y \in [0, 1], \\ u(1, t) = 0, v(1, t) = 0, \text{ for } t > 0 \text{ and } y = 1. \end{aligned} \quad (6.21)$$

6.3. Solution method

The two integral transforms, Laplace transform and finite Hankel transform, are used to find the analytic solutions of the time fractional derivatives (6.17) and (6.18), subject to the initial conditions and boundary conditions (6.21). The Laplace transform method is essentially used when the fluid model is described as a function of time. Applying the Laplace transform to Eqs. (6.17) and (6.18), and using initial conditions from Eq. (6.21) yields

$$\begin{aligned} \frac{s}{s + \alpha(1-s)} u(y, s) = & \left(q_0 \frac{1}{s} + q_1 \frac{s}{s^2 + \phi^2} \right) + \frac{1}{\text{Re}(1 + \lambda_1) R^2} \left(\frac{\partial^2}{\partial y^2} + \frac{1}{y} \frac{\partial}{\partial y} \right) u(y, s) \\ & + \frac{\text{pc}}{\text{Re}} v(y, s) - \left(\frac{\text{pc}}{\text{Re}} + \frac{1}{\text{Da Re}} + \text{Ha}^2 \right) u(y, s) \\ & + \ell_0 \left(\cos \gamma_0 \frac{s}{s^2 + k^2} - \sin \gamma_0 \frac{k}{s^2 + k^2} \right) + \frac{1}{s} g \sin \beta, \end{aligned} \quad (6.22)$$

$$p_m \frac{s}{s + \alpha(1-s)} v(y, s) = u(y, s) - v(y, s), \quad (6.23)$$

$$\text{with } u(1, s) = 0, v(1, s) = 0. \quad (6.24)$$

Solving for $v(y, s)$ from Eq. (6.23) yields

$$v(y, s) = \frac{s + \alpha(1-s)}{p_m s + s + \alpha(1-s)} u(y, s). \quad (6.25)$$

Upon substitution of Eq. (6.25) into Eq. (6.22), we get

$$\begin{aligned}
\frac{s}{s+\alpha(1-s)}u(y,s) &= \left(q_0 \frac{1}{s} + q_1 \frac{s}{s^2 + \varphi^2} \right) + \frac{1}{\text{Re}(1+\lambda_1)R^2} \left(\frac{\partial^2}{\partial y^2} + \frac{1}{y} \frac{\partial}{\partial y} \right) u(y,t) \\
&+ \left(\frac{\text{pc}}{\text{Re}} \left(\frac{s+\alpha(1-s)}{p_m s + s + \alpha(1-s)} \right) - \left(\frac{\text{pc}}{\text{Re}} + \frac{1}{\text{Da Re}} + \text{Ha}^2 \right) \right) u(y,s) \\
&+ \ell_0 \left(\cos \gamma_0 \frac{s}{s^2 + k^2} - \sin \gamma_0 \frac{k}{s^2 + k^2} \right) + \frac{1}{s} g \sin \beta.
\end{aligned} \tag{6.26}$$

Transformation of Eq. (6.26) using finite Hankel transform of order zero and application of BCs from Eq. (6.24) gives

$$\begin{aligned}
&\left(\frac{s}{s+\alpha(1-s)} - \frac{\text{pc}}{\text{Re}} \left(\frac{s+\alpha(1-s)}{p_m s + s + \alpha(1-s)} \right) + \frac{r_n^2}{\text{Re}(1+\lambda_1)R^2} + \frac{\text{pc}}{\text{Re}} + \frac{1}{\text{Da Re}} + \text{Ha}^2 \right) u_H(y_n, s) \\
&= \left(\left(q_0 \frac{1}{s} + q_1 \frac{s}{s^2 + \varphi^2} \right) + \ell_0 \left(\cos \gamma_0 \frac{s}{s^2 + k^2} - \sin \gamma_0 \frac{k}{s^2 + k^2} \right) + \frac{1}{s} g \sin \beta \right) \frac{J_1(y_n)}{y_n},
\end{aligned} \tag{6.27}$$

where, $u_H(y_n, s) = \int_0^1 y u(y, s) J_0(y y_n) dy$ is the HT of $u(y, s)$, with $y_n (n=1, 2, 3, \dots)$ are the positive roots of $J_0(\cdot)$. The functions $J_0(\cdot)$ and $J_1(\cdot)$ are the 0th and 1st order Bessel functions of the 1st kind.

Rearranging the coefficients of $u_H(y_n, s)$ in Eq. (6.27) yields

$$u_H(y_n, s) = \frac{a_{4n}s^2 + a_{5n}s + a_{6n}}{a_{8n}s^2 + a_{9n}s + a_{10n}} \left(\left(q_0 \frac{1}{s} + q_1 \frac{s}{s^2 + \varphi^2} \right) + \ell_0 \left(\cos \gamma_0 \frac{s}{s^2 + k^2} - \sin \gamma_0 \frac{k}{s^2 + k^2} \right) + \frac{1}{s} g \sin \beta \right) \frac{J_1(y_n)}{y_n}. \tag{6.28}$$

Applying the partial fraction decomposition of $\frac{a_{4n}s^2 + a_{5n}s + a_{6n}}{a_{8n}s^2 + a_{9n}s + a_{10n}}$ in Eq. (6.28) and simplifying the equation yields

$$u_H(y_n, s) = \left(\frac{a_{13n}}{s - a_{11n}} + \frac{a_{14n}}{s - a_{12n}} \right) \left(\begin{aligned} & \left((q_0 + g \sin \beta) \frac{1}{s} + q_1 \frac{s}{s^2 + \varphi^2} + \ell_0 \cos \gamma_0 \frac{s}{s^2 + k^2} \right) \frac{J_1(y_n)}{y_n} \\ & - \ell_0 \sin \gamma_0 \frac{k}{s^2 + k^2} \end{aligned} \right) \quad (6.29)$$

Expanding the coefficients of Eq. (6.29) yields

$$u_H(y_n, s) = \left(\begin{aligned} & (q_0 + g \sin \beta) \left[a_{13n} \frac{s^{-1}}{s - a_{11n}} + a_{14n} \frac{s^{-1}}{s - a_{12n}} \right] \\ & + q_1 \frac{s}{s^2 + \varphi^2} \left[a_{13n} \frac{1}{s - a_{11n}} + a_{14n} \frac{1}{s - a_{12n}} \right] \\ & + \ell_0 \cos \gamma \frac{s}{s^2 + k^2} \left[a_{13n} \frac{1}{s - a_{11n}} + a_{14n} \frac{1}{s - a_{12n}} \right] \\ & - \ell_0 \sin \gamma \frac{k}{s^2 + k^2} \left[a_{13n} \frac{1}{s - a_{11n}} + a_{14n} \frac{1}{s - a_{12n}} \right] \end{aligned} \right) \frac{J_1(y_n)}{y_n}, \quad (6.30)$$

where the corresponding parameters used in Eqs. (6.28) and (6.29) are given by

$$\begin{aligned} a_{1n} &= \text{Re}(p_m - \alpha + 1) - \text{pc}(1 - \alpha)^2, \quad a_{2n} = \alpha(\text{Re} - 2\text{pc}(1 - \alpha)), \quad a_{3n} = -\text{pc}\alpha^2, \\ a_{4n} &= \text{Re}(p_m(1 - \alpha) + (1 - \alpha)^2), \quad a_{5n} = \text{Re}\alpha(p_m + 2(1 - \alpha)), \quad a_{6n} = \text{Re}\alpha^2, \\ a_{7n} &= \frac{r_n^2 \text{Da} + (1 + \lambda_1) [R^2 \text{Da} (1 + \text{Pc} + \text{Re Ha}^2)]}{\text{Re Da} R^2 (1 + \lambda_1)}, \quad a_{8n} = a_{1n} + a_{4n} a_{7n}, \quad a_{9n} = a_{2n} + a_{5n} a_{7n}, \\ a_{10n} &= a_{3n} + a_{6n} a_{7n}, \quad a_{11n} = \left(\frac{-a_{9n} + \sqrt{a_{9n}^2 - 4a_{8n} a_{10n}}}{2a_{8n}} \right), \quad a_{12n} = \left(\frac{-a_{9n} - \sqrt{a_{9n}^2 - 4a_{8n} a_{10n}}}{2a_{8n}} \right), \\ a_{13n} &= \frac{a_{4n} a_{11n}^2 - a_{5n} a_{11n} + a_{6n}}{a_{11n} - a_{12n}}, \quad a_{14n} = \frac{a_{4n} a_{12n}^2 - a_{5n} a_{12n} + a_{6n}}{a_{12n} - a_{11n}}. \end{aligned} \quad (6.31)$$

To apply the inverse Laplace transform to Eqs. (6.30), the following special functions are used [75, 76]

$$L^{-1} \left[\frac{1}{s^\psi + \zeta} \right] = F_\psi(-\zeta, t) = \sum_{n=0}^{\infty} \frac{(-\zeta)^n t^{(n+1)\psi-1}}{\Gamma((n+1)\psi)}, \quad \psi > 0, \quad (6.32)$$

$$L^{-1}\left[\frac{s^{-\varepsilon}}{s^{\psi} + \zeta}\right] = \Re_{\psi, \varepsilon}(-\zeta, t) = \sum_{n=0}^{\infty} \frac{(-\zeta)^n t^{(n+1)\psi-1-\varepsilon}}{\Gamma((n+1)\psi - \varepsilon)}, \text{Re}(\psi - \varepsilon) > 0, \quad (6.33)$$

where, $F_{\psi}(-\zeta, t)$ and $\Re_{\psi, \varepsilon}(-\zeta, t)$ are the Robotnov-Hartley and Lorenzo-Hartley functions, respectively.

Upon the application of inverse Laplace transform to Eq. (6.30) with the help of Eqs. (6.32) and (6.33) yields

$$u_H(y_n, t) = [G_{11n}(t) + G_{22n}(t) + G_{33n}(t) + G_{44n}(t)] \frac{J_1(y_n)}{y_n}, 0 < \alpha < 1, \quad (6.34)$$

where,

$$\begin{aligned} G_{11n}(t) &= (q_0 + g \sin \beta) (a_{13n} R_{1,1}(a_{11n}, t) + a_{14n} R_{1,1}(a_{12n}, t)), \\ G_{22n}(t) &= q_1 (\cos(\varphi t) * [a_{13n} F_1(a_{11n}, t) + a_{14n} F_1(a_{12n}, t)]), \\ G_{33n}(t) &= \ell_0 \cos \gamma (\cos(kt) * [a_{13n} F_1(a_{11n}, t) + a_{14n} F_1(a_{12n}, t)]), \\ G_{44n}(t) &= -\ell_0 \sin \gamma (\sin(kt) * [a_{13n} F_1(a_{11n}, t) + a_{14n} F_1(a_{12n}, t)]). \end{aligned} \quad (6.35)$$

Applying the inverse HT to Eq. (6.34) yields the velocity of blood, which has the form

$$u(y, t) = 2 \sum_{n=1}^{\infty} \frac{J_0(y y_n)}{y_n J_1(y_n)} [G_{11n}(t) + G_{22n}(t) + G_{33n}(t) + G_{44n}(t)]. \quad (6.36)$$

The magnetic nanoparticles velocity can be determined from Eq. (6.25) by using inverse Laplace transform.

$$L^{-1}[v(y, s)] = L^{-1}\left[\frac{\alpha + s(1-\alpha)}{\alpha + s(p_m + 1 - \alpha)} u(y, s)\right]. \quad (6.37)$$

Simplification of Eq. (6.37) yields

$$v(y, t) = a_{15n} (1 - a_{16n}) [F_1(-a_{15n}, t) * u(y, t)], 0 < \alpha < 1. \quad (6.38)$$

The constants used in Eq. (6.38) are

$$a_{15n} = \frac{\alpha}{p_m + (1-\alpha)}, a_{16n} = \frac{1-\alpha}{p_m + (1-\alpha)}. \quad (6.39)$$

The symbol $*$ in Eqs. (6.35) and (6.38) represents the convolution product, where

$$(h * g)(t) = \int_0^t h(\tau)g(t-\tau)d\tau \text{ shows the convolution of two functions } h \text{ and } g.$$

The wall shear stress of the flow field can be calculated from

$$\tau_w = -\frac{\mu}{\Lambda} \left(\frac{1}{1+\lambda_1} \right) \left(\frac{\partial u}{\partial r} \Big|_{r=R} \right). \quad (6.40)$$

The skin friction of the flow field in dimensionless form is

$$C_f(z, t) = \frac{\tau_w}{\rho u_0^2} = \frac{2}{\text{Re}(1+\lambda_1)R} \sum_{n=1}^{\infty} [G_{11n}(t) + G_{22n}(t) + G_{33n}(t) + G_{44n}(t)], \quad (6.41)$$

where, $u_0 = R_0/\Lambda$ is the characteristic velocity.

The pressure drops between $z = 0$ and $z = L$ through the stenosis channel can be written as

$$\Delta p = \int_0^L \left(-\frac{\partial p}{\partial z} \right) dz. \quad (6.42)$$

The flow rate Q and the impedance λ (flow resistance) can respectively be written as follows:

$$\begin{aligned} Q(z, t) &= 2\pi \int_0^R ru(r, t) dy = 2\pi R^2 \int_0^1 yu(y, t) dy \\ &= 4\pi R^2 \sum_{n=1}^{\infty} \frac{1}{y_n^2} [G_{11n}(t) + G_{22n}(t) + G_{33n}(t) + G_{44n}(t)], \end{aligned} \quad (6.43)$$

$$\lambda(z, t) = \frac{\Delta p}{Q(z, t)} = \frac{1}{Q(z, t)} \left[\int_0^d \left(-\frac{\partial p}{\partial z} \right) dz + \int_d^{d+L_0} \left(-\frac{\partial p}{\partial z} \right) dz + \int_{d+L_0}^L \left(-\frac{\partial p}{\partial z} \right) dz \right]_{R=1}. \quad (6.44)$$

Eq. (6.44) simplifies to

$$\lambda(z,t) = \frac{\Delta p}{Q(z,t)} = \frac{1}{Q(z,t)} \left[(L - L_0)(q_0 + q_1 \cos(\varphi t))_{R=1} + \int_d^{d+L_0} (q_0 + q_1 \cos(\varphi t)) dz \right]. \quad (6.45)$$

6.4. Results and discussion

In the present study, the non-Newtonian Jeffrey fluid flow of blood with the transport of magnetic nanoparticles is analyzed to explore meaningful interpretations. The governing equations are solved by using integral transforms. Eqs. (6.36), (6.38), (6.41), (6.43) and (6.45) represent the velocity of blood $u(y,t)$, velocity of magnetic nanoparticles $v(y,t)$, skin friction $C_f(z,t)$, volumetric flow rate $Q(z,t)$, and flow resistance $\lambda(z,t)$, respectively. Corresponding to these analytic solutions, we present the graphs for $u(y,t)$, $v(y,t)$, $C_f(z,t)$, $Q(z,t)$ and $\lambda(z,t)$ by applying the use of MATLAB simulations, and the results are demonstrated in Figs. 6-3 – 6-13. These graphs demonstrate the impacts of fractional parameter α , Darcy number Da , Jeffrey fluid parameter λ_1 , stenosis height δ , inclination angle β , Hartmann number Ha , shape parameter W , and magnetic nanoparticles concentration parameter pc in the stenosis region. A set of values for the parameters for the present study is considered from existing literature, and it is shown in Table 6 -1.

Table 6 - 1 Physical parameter values with references.

Physical parameters	Values	References
p_m	0.8	Maiti et al. [129]
γ_o	$\pi/3$	Maiti et al. [129]
pc	0.5	Maiti et al. [129]
φ	$\pi/4$	Ali et al. [254]
Re	3	Ali et al. [254]
k	$\pi/4$	Bansi et al. [126]
Da	0.8	Yadeta and Shaw [127]
W	2	Ponalagusamy [252]

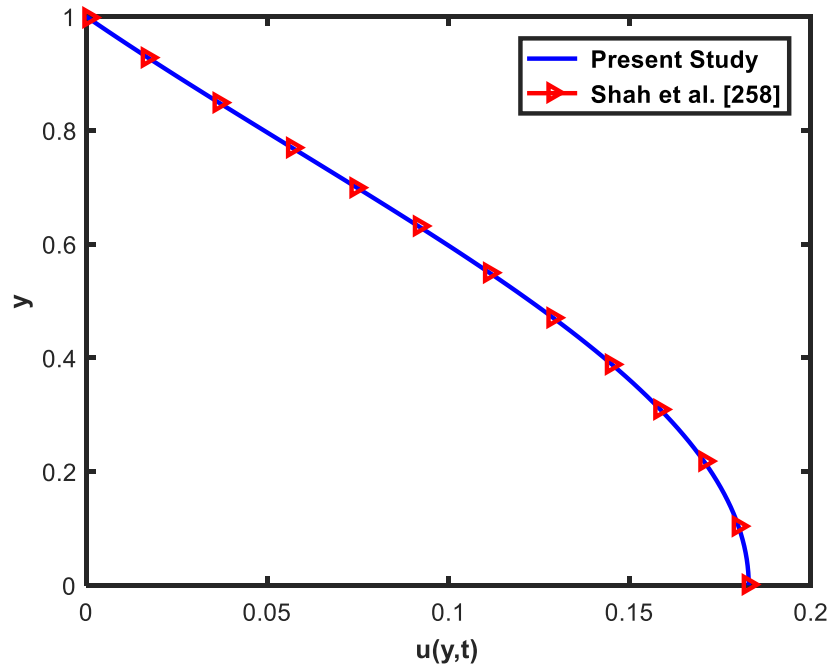


Figure 6.2 Comparison of velocity profile with the works of Shah et al. [258].

Table 6 - 2 Comparison of velocity profile with the works of Shah et al. [258].

Parameters	$\lambda_1 = \beta = \ell_0 = 0, \text{Da} \rightarrow \infty, q_0 = 0.5, q_1 = 0.6,$ $p_m = 0.8, p_c = 0.5, \text{Re} = 5, \varphi = \pi/4, \text{Ha} = 2, z = 1$	
y	Shah et al. [256]	Present Study
0.00	0.182914	0.182916
0.10	0.180279	0.180281
0.20	0.172488	0.172490
0.35	0.151425	0.151427
0.50	0.122540	0.122541
0.59	0.102235	0.102236
0.60	0.099404	0.099405
0.70	0.074552	0.074553
0.80	0.049014	0.049014
0.90	0.023829	0.023829
1.00	0.000000	0.000000

To indicate the symmetric nature of stenosis the value of shape factor $w=2$ is used. Magnetic nanoparticles concentration ($pc=0.5$) is just used to keep the velocity of magnetic nanoparticles at normal condition without causing exaggerated skin friction under applied magnetic field. The physical meaning of the remaining parameters in the table are given in section 4.10. The validation of the present result is in excellent agreement with the Newtonian fluid (works of Shah et al. [258]) for $\lambda_1 = \beta = \ell_0 = 0$, $Da \rightarrow \infty$, $q_0 = 0.5$, $q_1 = 0.6$, $p_m = 0.8$, $pc = 0.5$, $Re = 5$, $\varphi = \pi/4$, $Ha = 2$, $z = 1$ and the results are shown in Fig. 6.2 and Table 6 -2.

6.4.1. Effect of fractional parameter

A time-variant C-F fractional derivative concept, which gives the memory impact, is utilized in the governing equations of blood flow and transport of nanoparticles. The final solutions of the flow pattern with the corresponding physical quantities are displayed along with the fractional parameter. The present analysis considers a wide range of the values of parameter α with ($\alpha=0.4, 0.6, 0.8, 1.0$). The lower value of α (i.e, $\alpha=0.4$) supports the lower memory effect, while the larger value of α ($\alpha=0.8$) supports the higher memory impact. The general time derivative is represented by $\alpha=1.0$. In all the results displayed graphically, the effect of the variation of fractional parameters is incorporated, which reflects a tremendous contribution to the flow field and physical quantities. Figs. 6.3 and 6.4 show the impact of the fractional parameters on the velocities of fluid and magnetic nanoparticles along with different values of Darcy number Da , and Jeffrey fluid parameter λ_1 . From the figures it is shown that the fractional parameters support the flow of blood and the transport of magnetic nanoparticles. Hence, the velocities of blood and magnetic nanoparticles increase with increase in α . It is seen that the larger value of memory effect ($\alpha=0.8$) accelerates the flow of blood and the transport of magnetic nanoparticles, and the phenomenon continues for the general time derivative with $\alpha=1.0$. On the other hand, a smaller value of α slows the velocities of both blood and magnetic nanoparticles, and the velocities are quickly dropped. This phenomenon is supported by the behavior of fractional parameters. Hence, a large value of α gives a quick response to the previous memories of blood flow behavior and the transport of magnetic nanoparticles, whereas the lower value of α takes some intermediate time to respond. Since, it is shown that α plays an imperative role in regulating both the velocities. It is important to mention that although the velocity profile for magnetic

nanoparticles shows the same trend as the velocity of blood, there is a significant difference in the magnitude of the velocities. The transport velocity of magnetic nanoparticles is comparatively lower when compared to the velocity of blood. This happens due to the additional impact of retarding and drag forces on the magnetic nanoparticles [254].

Fig. 6-5 depicts the influence of the fractional parameters α on volumetric flow rate Q for different values of stenosis height δ . From the figure, the volumetric flow rate slows down for a lower value of the fractional parameter and speeds up for a higher value of the fractional parameter, which supports a long memory effect. This phenomenon happens due to the fact that the volumetric flow rate has a positive correlation with the velocity of the fluid. Figs 6.6 and 6.7 depict the influence of α on flow resistance λ , for different values of Hartman number Ha and stenosis height δ , respectively. From both figures, it is shown that the flow resistance decreases with an increase in the value of the fractional parameter. From Figs. 6-6 and 6-7, it is clearly indicated that the larger fractional parameter that supports the long memory effect restricts the passage of fluid through the stenosis region more than the lower fractional parameter that supports the short memory effect. Hence, the flow resistance phenomenon is inversely proportional to the volumetric flow rate, which is why the impact of fractional parameters shows such an inverse relation to flow resistance. The impacts of α along with shape parameter W , Jeffrey fluid parameter λ_1 and magnetic nanoparticles concentration parameter pc on skin friction C_f of the inner arterial wall are demonstrated in Figs 6-8, 6-9 and 6-10, respectively. From the figures, it is observed that the value of skin friction is higher for the larger fractional parameter that supports the long memory effect, whereas the lower fractional parameter that supports the short memory effect restricts skin friction. In physical terms, the skin friction is supported by the increase in the velocity field of the fluid, as observed in Fig. 6.3. One can clearly understand that the findings from Figs. 6.3 – 6.10 show the advantage of using the time fractional derivative model in real-life applications. A proper selection of fractional order parameter α which links to the flow of blood and the transport of magnetic nanoparticles is a key factor that can be applicable in the medical science field for local drug targeting purposes to treat diseases such as atherosclerosis and tumor cells. Further, the application can reduce bleeding during surgery.

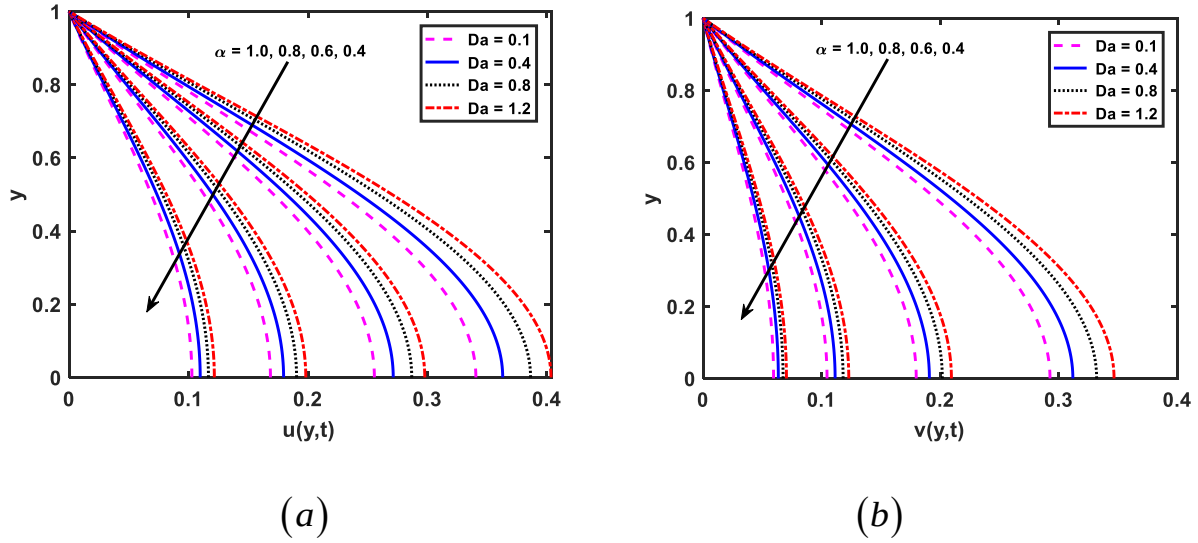


Figure 6.3 Profiles of the velocities (a) $u(y,t)$ and (b) $v(y,t)$ for different Da and α when $\lambda_1 = 0.6$, $q_0 = 0.2$, $q_1 = 0.3$, $\ell_0 = 0.8$, $\beta = \pi/6$, $L = 5$, $d = 1$, $L_0 = 2$, $\delta = 0.08$, $t = 0.3$ and $g = 9.81$.

6.4.2. Distribution of velocities

Fig. 6-3 demonstrates the impact of Darcy number Da and α on the velocities of blood and magnetic nanoparticles. The Darcy number Da is related to the permeability nature of the vessel and it significantly affects the velocities of blood and magnetic nanoparticles. From the figure, it is illustrated that both velocities increase with an increase in Da . Physically, this condition is associated with factors such as the permeability of the artery and the intravascular pressure, which contribute to blood flow. On the other hand, when the permeability of the medium increases, the drag force decreases, which in turn increases the velocities of blood and magnetic nanoparticles. From these phenomena, it can be claimed that the arterial wall with lower permeability supports the capture efficiency of the drug particles better than the artery with higher permeability. This shows the importance of the permeability of the arterial wall in regulating the velocities to trap the magnetic nanoparticles in the diseased region during drug targeting.

Visco-elastic fluids are non-Newtonian fluids that exhibit both viscous and elastic components in nature. The viscous components arise due to the presence of plasma, while the presence of red blood cells (RBCs) is responsible for the elastic nature [259]. Further, it is clear that the higher

hematocrit (percentage of RBCs in the blood) enhances the elastic nature of the blood, particularly in small blood vessels [65]. In the present study, Jeffrey fluid is used to define the rheology of blood due to its viscoelastic nature. Fig. 6.4 demonstrates the impact of Jeffrey fluid parameter λ_1 along with α on velocities of blood and magnetic nanoparticles. From the figure, it is seen that both the velocities of blood and magnetic nanoparticles increase with increases in the value of λ_1 . This means that larger value of λ_1 leads to higher relaxation time that allows more time for the fluid and magnetic nanoparticles to move faster. This parameter has a vital role in regulating blood flow and can be applicable during drug delivery phenomena and surgery [241].

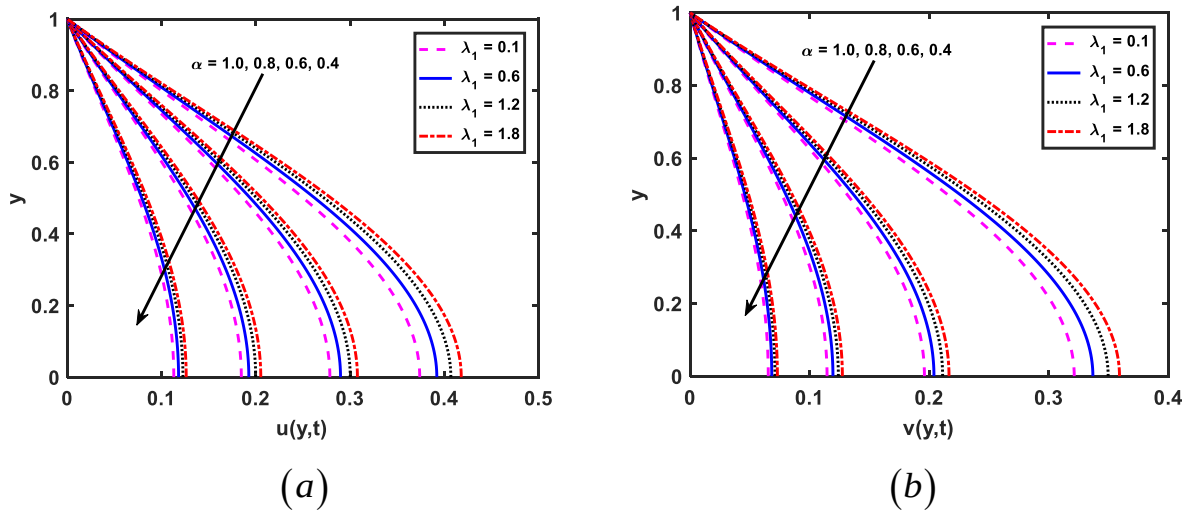


Figure 6.4 Profiles of the velocities (a) $u(y,t)$ and (b) $v(y,t)$ for different λ_1 and α when, $q_0 = 0.2$, $q_1 = 0.3$, $\ell_0 = 0.8$, $\beta = \pi/6$, $L = 5$, $d = 1$, $L_0 = 2$, $\delta = 0.08$, $t = 0.3$ and $g = 9.81$.

6.4.3. Distribution of volumetric flow rate

Figs. 6.5 and 6.6 display the graphs of volumetric flow rate Q with respect to the axial distance for different values of stenosis height δ (along with α), and inclination angle β , respectively. The volume flow rate represents the volume of fluid that passes through a particular region of the vessel per unit of time. It is well known that the volumetric flow rate is proportional to the cross-sectional area of the vessel and the velocity of the fluid. Due to the presence of stenosis, the cross-sectional area of the blood vessel changes. Furthermore, the volumetric flow rate through a blood vessel is highly affected by the change in the radius of the vessel due to the existence of stenosis

height. From Fig. 6.5, one can see that Q significantly decreases with increase in stenosis height. Hence, with an increase in $\mathcal{D}$, the radius of the artery in the stenosis region decreases, and further, the cross-sectional area of the artery decreases which is responsible for the reduction of Q . In physical terms, a reduction in the volumetric flow rate of blood can cause complications in the cardiovascular system, leading to stroke, heart attack, and so forth. The phenomenon can help biomedical engineers develop suitable devices to diagnose and treat atherosclerosis during drug targeting. From figure 6.6 it is shown that the volumetric flow rate enhances with increase in inclination angle β from $\beta = \pi/9$ to $\beta = \pi/3$. The volumetric flow rate is minimum when the blood vessel has lower inclination; however, the flow rate attains its maximum value at the maximum inclination angle. This phenomenon is related to the velocity of blood; hence, inclination angle is positively related to the velocity of blood flow.

6.4.4. Distribution of flow resistance

Figs. 6.7 and 6.8 depict the influence of Hartmann number Ha and stenosis height $\mathcal{D}$ along with α on the flow resistance λ , respectively. Among the primary factors that describe the resistance to the flow of blood is the change in vessel diameter. For example, vessel diameter changes when the fatty substance is built up in the internal lining of the vessel, which causes a cardiovascular disorder commonly known as stenosis. The presence of stenosis significantly enhances the flow resistance of blood [260]. In both figures (Figs. 6.7 and 6.8), it is seen that the stenosis is symmetric (with shape factor $w=2$) and hence the profile of the flow resistance is symmetric along the center of stenosis ($z=2$). Since, we only considered the stenosis region in the figure to show a clear impact of the flow resistance.

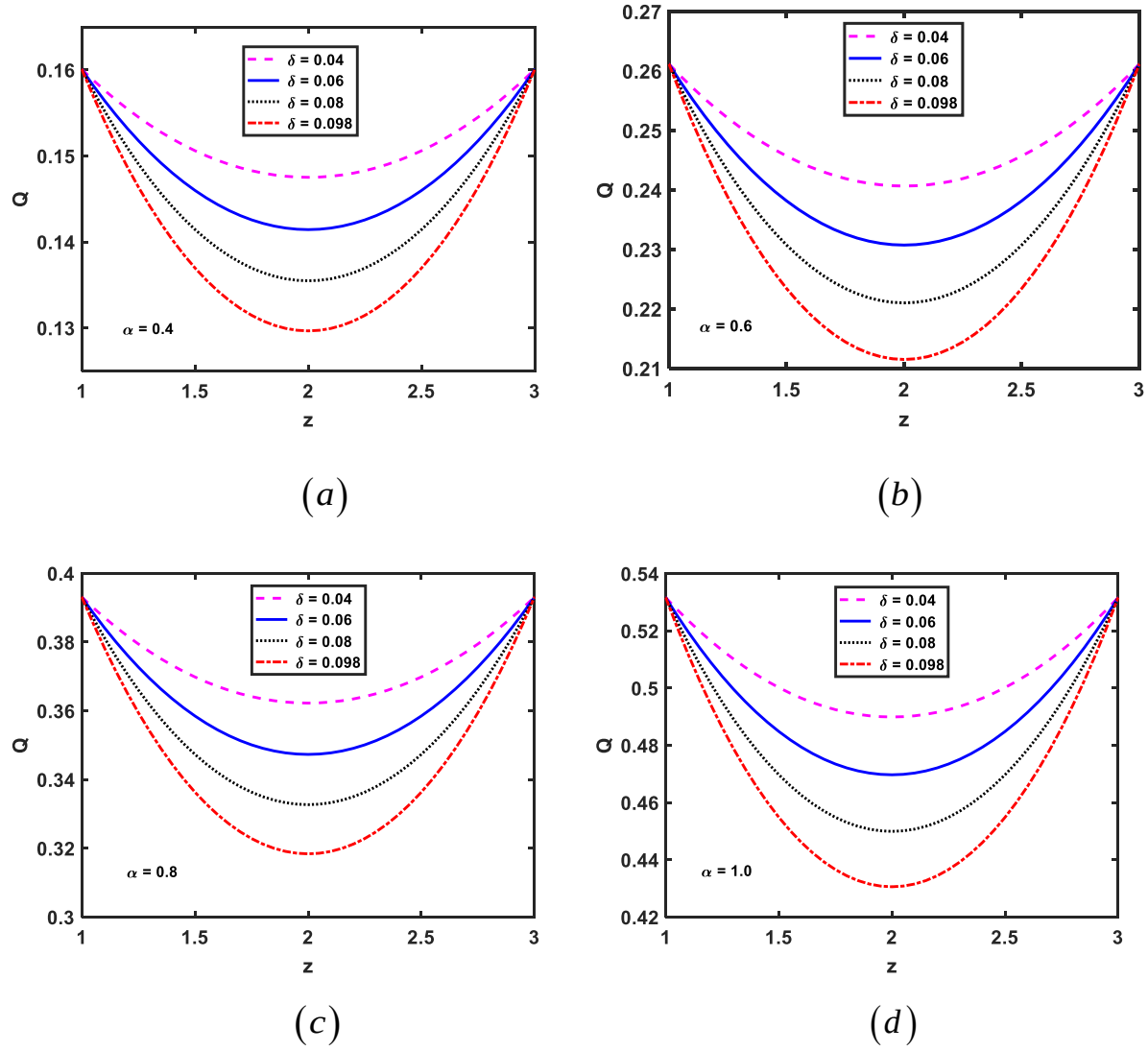


Figure 6.5 Profile of volumetric flow rate Q for different δ with $\lambda_1 = 0.6$, $q_0 = 0.2$, $q_1 = 0.3$, $\ell_0 = 0.8$, $\beta = \pi/6$, $L = 5$, $d = 1$, $L_0 = 2$, $t = 0.3$, and $g = 9.81$ when (a) $\alpha = 0.4$, (b) $\alpha = 0.6$, (c) $\alpha = 0.8$, (d) $\alpha = 1.0$.

Fig. 6.7 depicts the graph of the flow resistance against the axial distance for different values of Ha . When the fluid is under the impact of an applied magnetic field, the Hartman number Ha is considerably increases when the intensity of the Lorentz force increases. The increase in Ha tends to slow down the velocity of flow and enhance the flow resistance. Therefore, an essential,

regulated magnetic field is required for therapeutic applications to increase the capture efficiency of magnetic nanoparticles close to the atherosclerosis region [255].

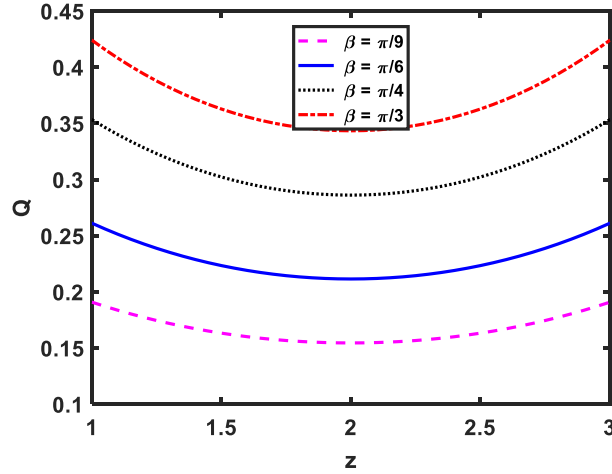
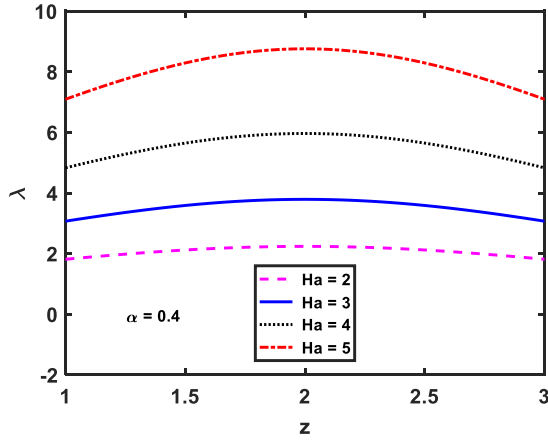


Figure 6.6 Profile of volumetric flow rate Q for different β when $\alpha = 0.6$, $\lambda_1 = 0.6$, $q_0 = 0.2$,

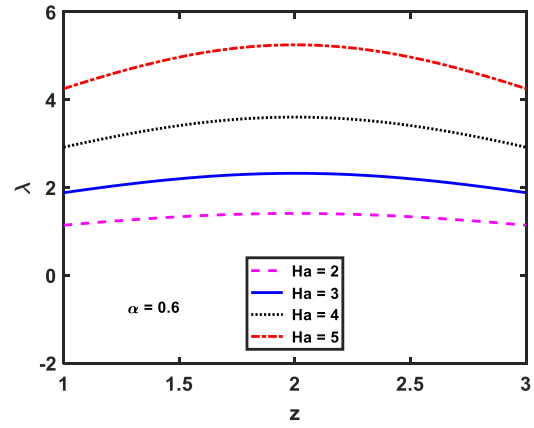
$$q_1 = 0.3, \ell_0 = 0.8, \beta = \pi/6, L = 5, d = 1, L_0 = 2, \delta = 0.08, t = 0.3, \text{ and } g = 9.81.$$

Fig. 6.8 shows the effect of stenosis height δ on the flow resistance λ . The flow resistance of a fluid is inversely proportional to the flow rate of the fluid as shown in Eq. (6.45). From the figure it is shown that the flow resistance λ significantly increases with enhancement in stenosis height. Hence, the flow resistance is considerably larger at the peak of the stenosis where the height of the stenosis is maximum. Therefore, it is important to analyze and characterize the impact of δ on the flow resistance λ , that will help the medical field to carry out further research to therapy atherosclerosis.

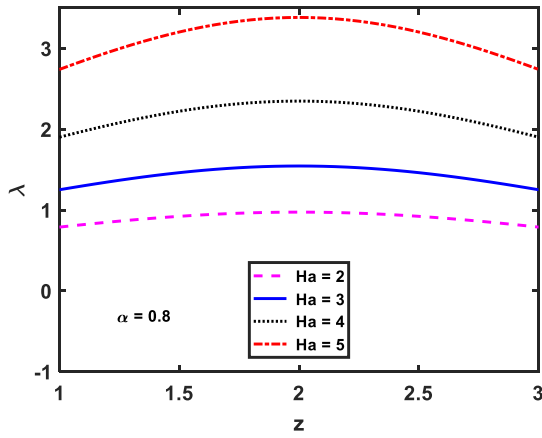
Fig. 6.9 displays the graph of flow resistance with respect to axial distance for different values of inclination angle β . From the figure it is seen that the flow resistance significantly decreases with enhancement in inclination angle. Hence, an opposite trend of inclination angle on volumetric flow rate is observed.



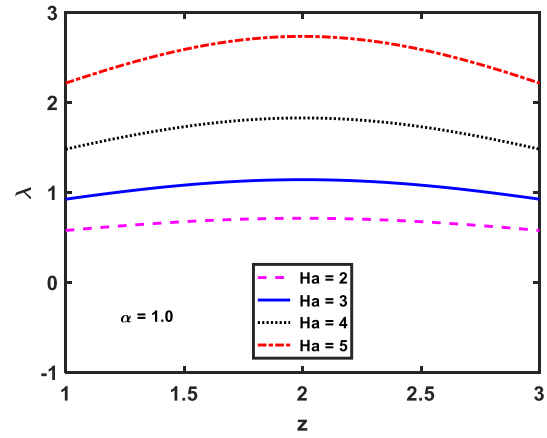
(a)



(b)



(c)



(d)

Figure 6.7 Profile of flow resistance λ for different Ha with $\lambda_1 = 0.6$, $q_0 = 0.2$, $q_1 = 0.3$, $\ell_0 = 0.8$, $\beta = \pi/6$, $L = 5$, $d = 1$, $L_0 = 2$, $\delta = 0.08$, $t = 0.3$, and $g = 9.81$ when (a) $\alpha = 0.4$

(a) $\alpha = 0.4$, (b) $\alpha = 0.6$, (c) $\alpha = 0.8$, (d) $\alpha = 1.0$.

6.4.5. Distribution of skin friction

Basically, skin friction is a physical quantity that appears due to the viscous nature of the fluid and measures the resistance of the fluid at the surface. It arises due to the wall shear stress formed by the fluid flow tangential to the inner wall of the artery. For laminar fluid flow and without any deformation of the artery, the skin friction is uniform. However, due to variations in wall thickness

or the presence of stenosis, skin friction may significantly affect the arterial wall. The generation of maximum shearing at the inner wall of the artery may lead to an aneurysm and damage the arterial wall [253]. Therefore, it is beneficial to understand, analyze, and characterize the nature of skin friction.

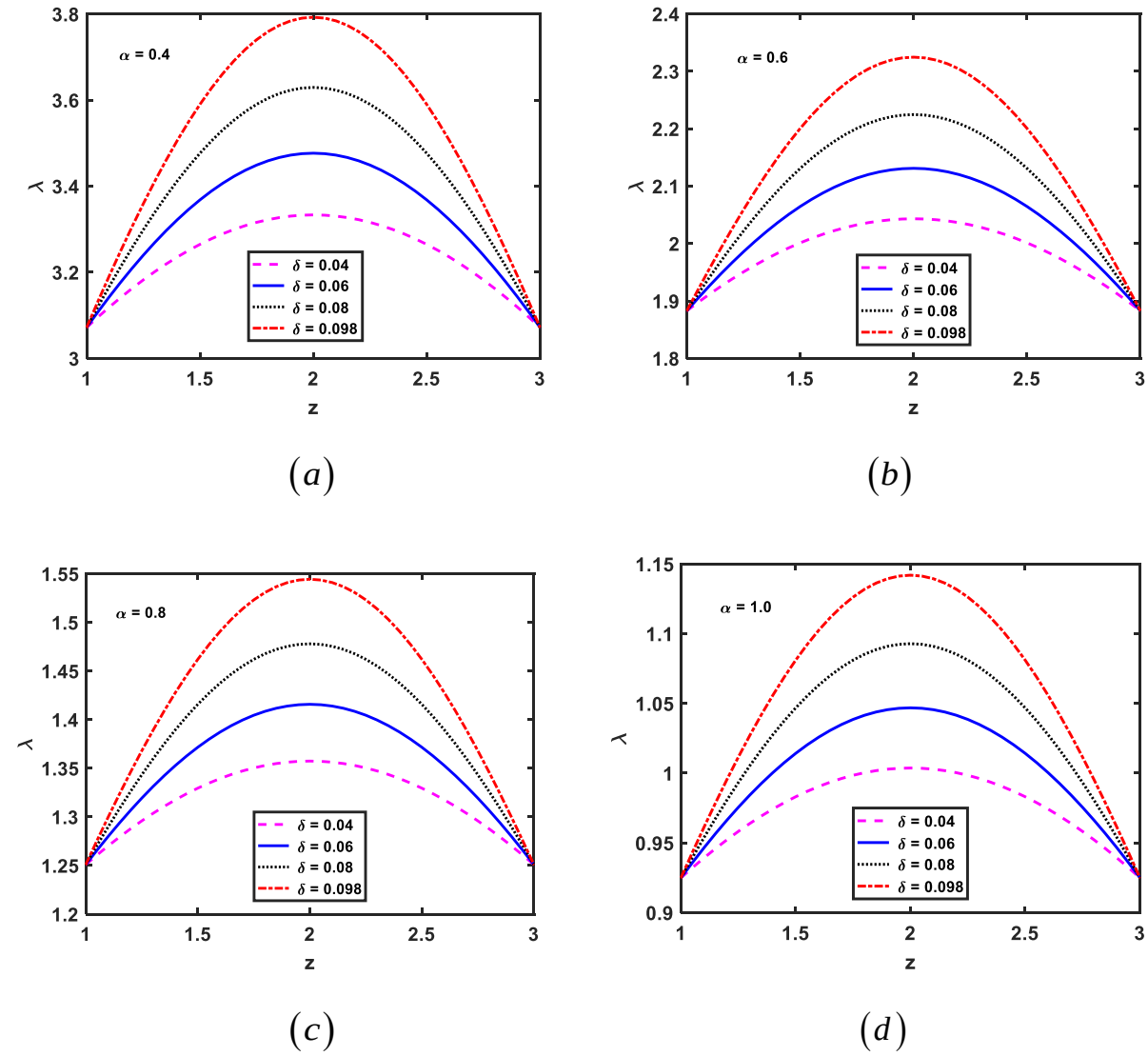


Figure 6.8 Profile of flow resistance λ for different δ with $\lambda_1 = 0.6$, $q_0 = 0.2$, $q_1 = 0.3$,

$\ell_0 = 0.8$, $\beta = \pi/6$, $L = 5$, $d = 1$, $L_0 = 2$, $t = 0.3$, and $g = 9.81$ when (a) $\alpha = 0.4$, (b)

$\alpha = 0.6$, (c) $\alpha = 0.8$, (d) $\alpha = 1.0$.

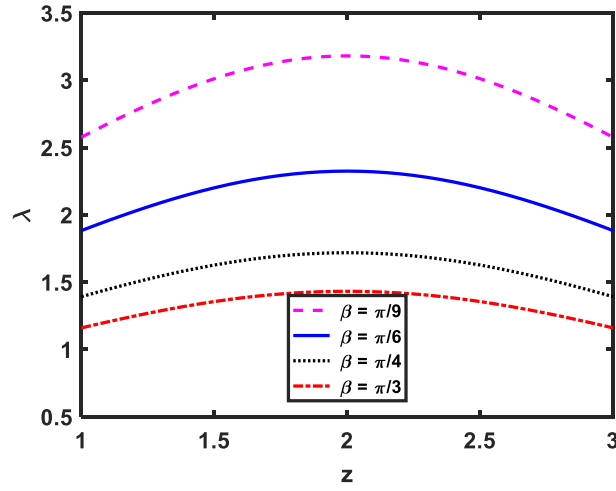


Figure 6.9 Profile of flow resistance λ for different β when $\alpha = 0.6$, $\lambda_1 = 0.6$, $q_0 = 0.2$, $q_1 = 0.3$, $\ell_0 = 0.8$, $\beta = \pi/6$, $L = 5$, $d = 1$, $L_0 = 2$, $\delta = 0.08$, $t = 0.3$, and $g = 9.81$.

Fig. 6.10 depicts the graph of skin friction C_f versus axial distance for different values of stenosis shape parameter w along with α . It is important to note that stenosis shows a symmetric shape with $w = 2$ and the non-symmetric nature is to appear for the other values of w . A symmetric nature of the stenosis shows a higher skin friction, whereas the skin friction reduces with enhancement in other values of the shape parameter W of the stenosis. Hence, the variation of the stenosis shape significantly changes the value of skin friction. Moreover, the profile of the skin friction resembles the shape of stenosis, and it is larger at the peak of the stenosis. On the other hand, we may conclude that the blood flow restriction is more because of the symmetric nature of stenosis than the non-symmetric shapes.

Fig. 6.11 depicts the graph of skin friction of the arterial wall with respect to axial distance for different values of λ_1 . From the figure it is demonstrated that the skin friction C_f decreases with enhancement in Jeffrey fluid parameter. This happens due to the fact that the Jeffrey fluid parameter is inversely proportional to skin friction. This phenomenon shows that blood rheology significantly influences the skin friction of the arterial wall of the stenosis region. Fig. 6.12 shows

the influence of inclination angle β on the skin friction of the arterial wall. It is demonstrated that the skin friction of the arterial wall boosts with enhancement in inclination angle.

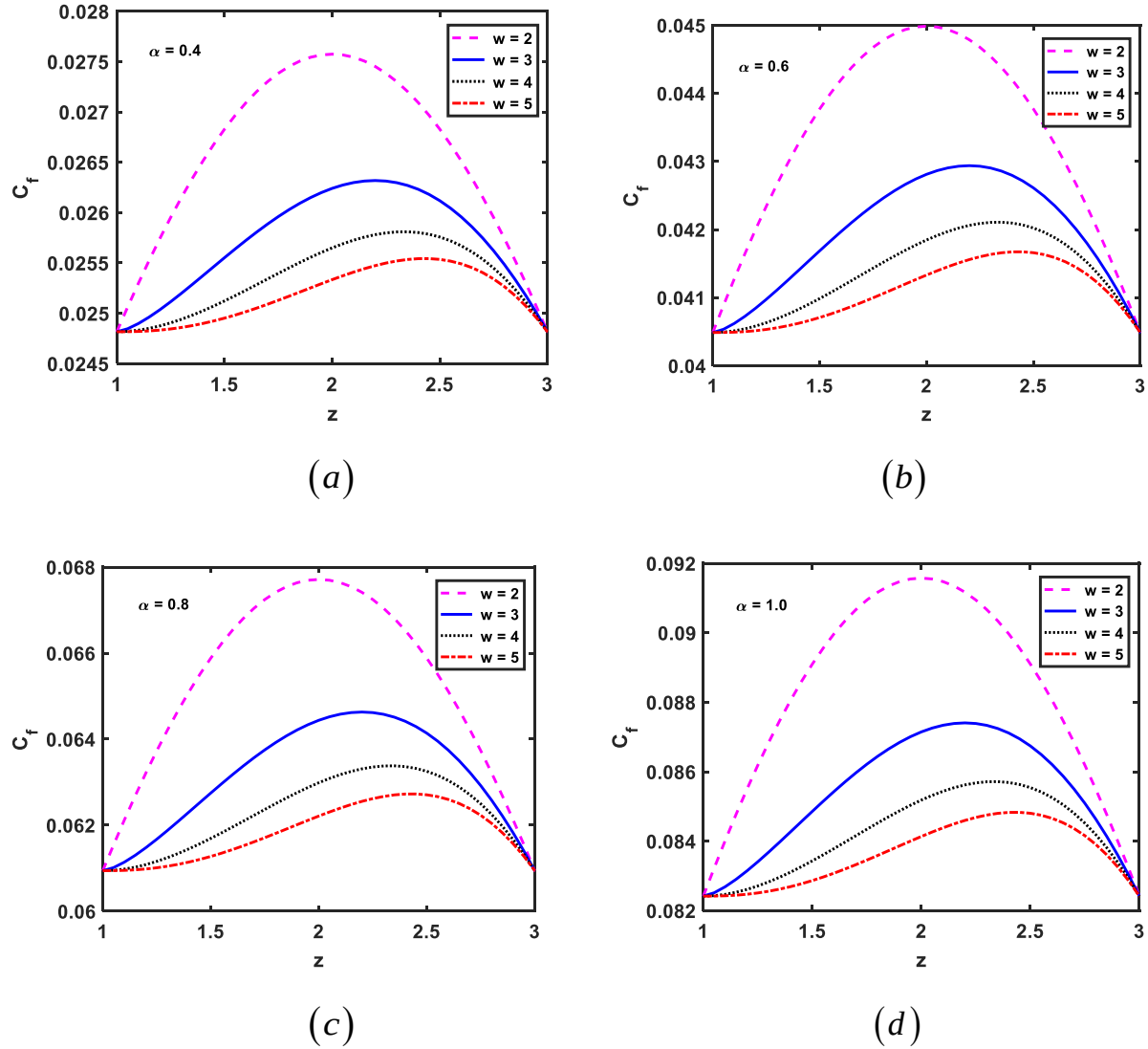


Figure 6.10 Profile of skin friction C_f for different w with $\lambda_1 = 0.6$, $q_0 = 0.2$, $q_1 = 0.3$, $\ell_0 = 0.8$, $\beta = \pi/6$, $L = 5$, $d = 1$, $L_0 = 2$, $\delta = 0.08$, $t = 0.3$ and $g = 9.81$ when (a) $\alpha = 0.4$, (b) $\alpha = 0.6$, (c) $\alpha = 0.8$, (d) $\alpha = 1.0$.

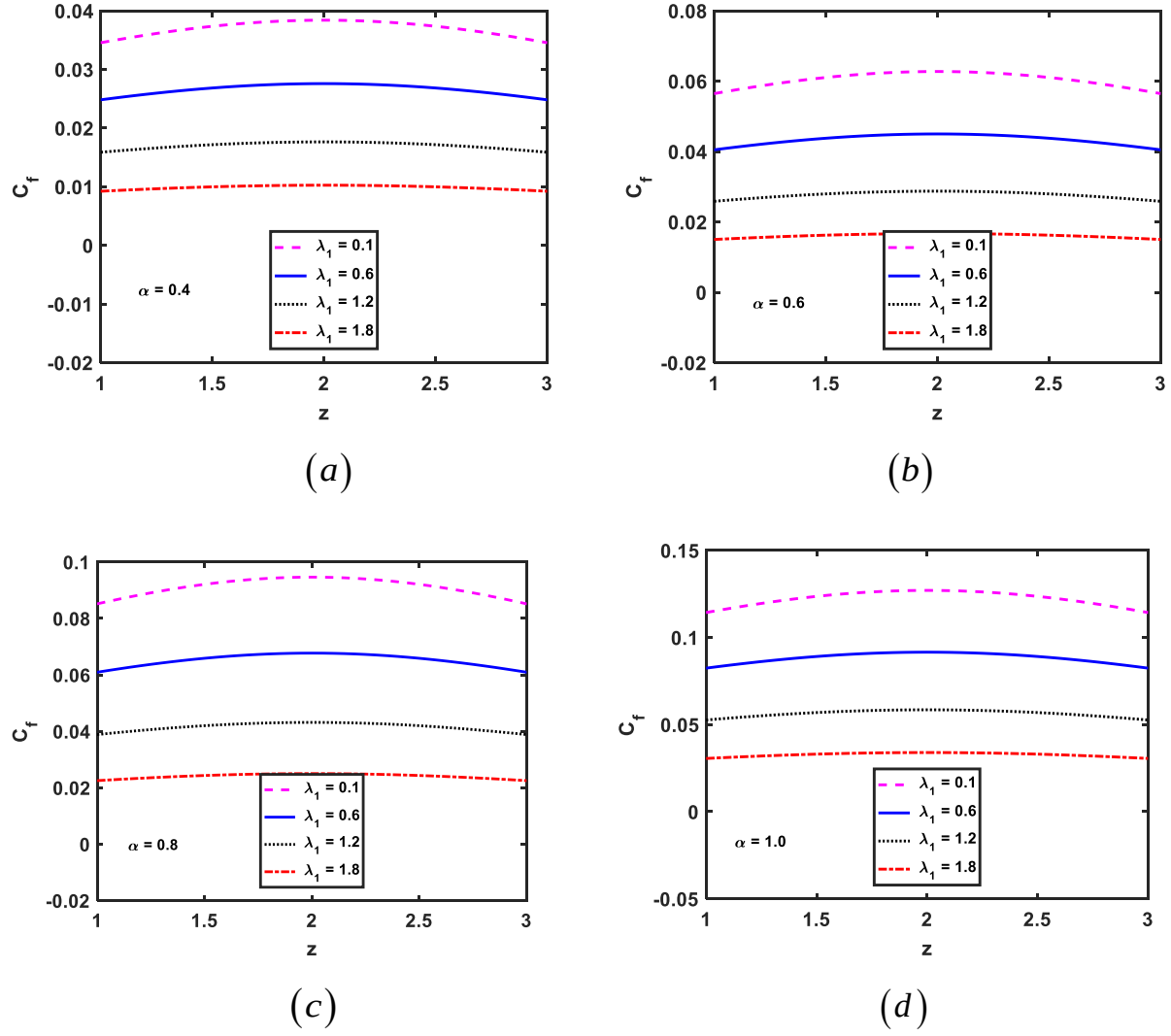


Figure 6.11 Profile of skin friction C_f for different λ_1 with $q_0 = 0.2$, $q_1 = 0.3$, $\ell_0 = 0.8$, $\beta = \pi/6$, $L = 5$, $d = 1$, $L_0 = 2$, $\delta = 0.08$, $t = 0.3$, and $g = 9.81$ when (a) $\alpha = 0.4$, (b) $\alpha = 0.6$, (c) $\alpha = 0.8$, (d) $\alpha = 1.0$.

Fig. 6.13 demonstrates the graph of skin friction C_f with respect to axial distance for different values of concentration of magnetic nanoparticles pc along with α . Nanoparticles have various applications in medicine and the bioengineering fields. Some of the applications include tumor destruction by means of heating (hyperthermia treatment) [260], separation and purification of biological molecules and cells [261], and drug and gene delivery [263, 264]. During the drug delivery phenomenon, the dose of drug concentration accumulated in the disease region plays a

crucial role in recovering the malignant tissue. In this direction, the controlled-release drug delivery system has an advantage over the conventional drug delivery system. Because in conventional drug delivery systems, the drugs are distributed randomly, are less absorbed, and damage unaffected areas [265].

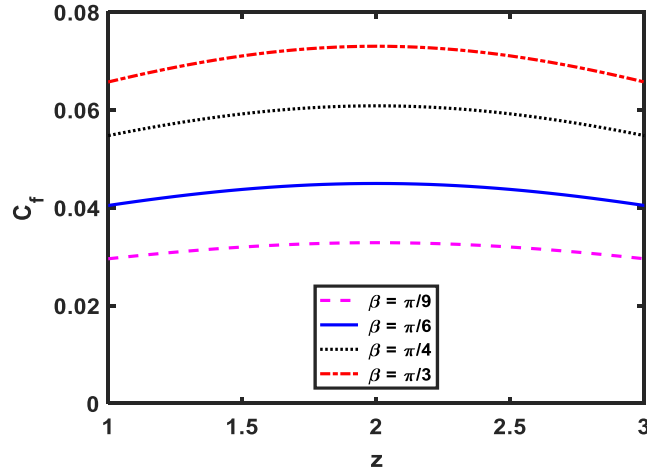


Figure 6.12 Profile of skin friction C_t for different β when $\alpha = 0.6$, $\lambda_1 = 0.6$, $q_0 = 0.2$, $q_1 = 0.3$, $\ell_0 = 0.8$, $\beta = \pi/6$, $L = 5$, $d = 1$, $L_0 = 2$, $\delta = 0.08$, $t = 0.3$ and $g = 9.81$.

In our work, we would like to know the effect of magnetic nanoparticles concentration on the skin friction of the arterial wall of the stenosis region. From Fig. 6.13, it is shown that the skin friction significantly increases with a boost in magnetic nanoparticles concentration because, during the application of a magnetic field, the particles concentration enhances the viscosity of the suspension [253]. The increase in viscose force dominates the velocity of magnetic particles which decreases due to this force and results in the enhancement of skin friction. Hence, this phenomenon tells us the advantage of magnetic nanoparticles concentration in regulating the flow velocity during drug transport through the artery and hence its capture efficiency in the stenosis region. In addition, it is worth mentioning that the percentage of increase of skin friction at the midpoint of the stenosis is 0.66%, 0.59%, 0.42%, and 0.13% for the fractional parameters (memory effects) $\alpha = 0.4$, $\alpha = 0.6$, $\alpha = 0.8$ and integer order $\alpha = 1.0$, respectively. The percentage increase in skin friction for the short memory effect is significantly higher than the long memory effect. On the other hand, it is important to note that for a particular value of the magnetic nanoparticles' concentration

parameter, the skin friction outside the stenosis region in the artery remains constant without variation.

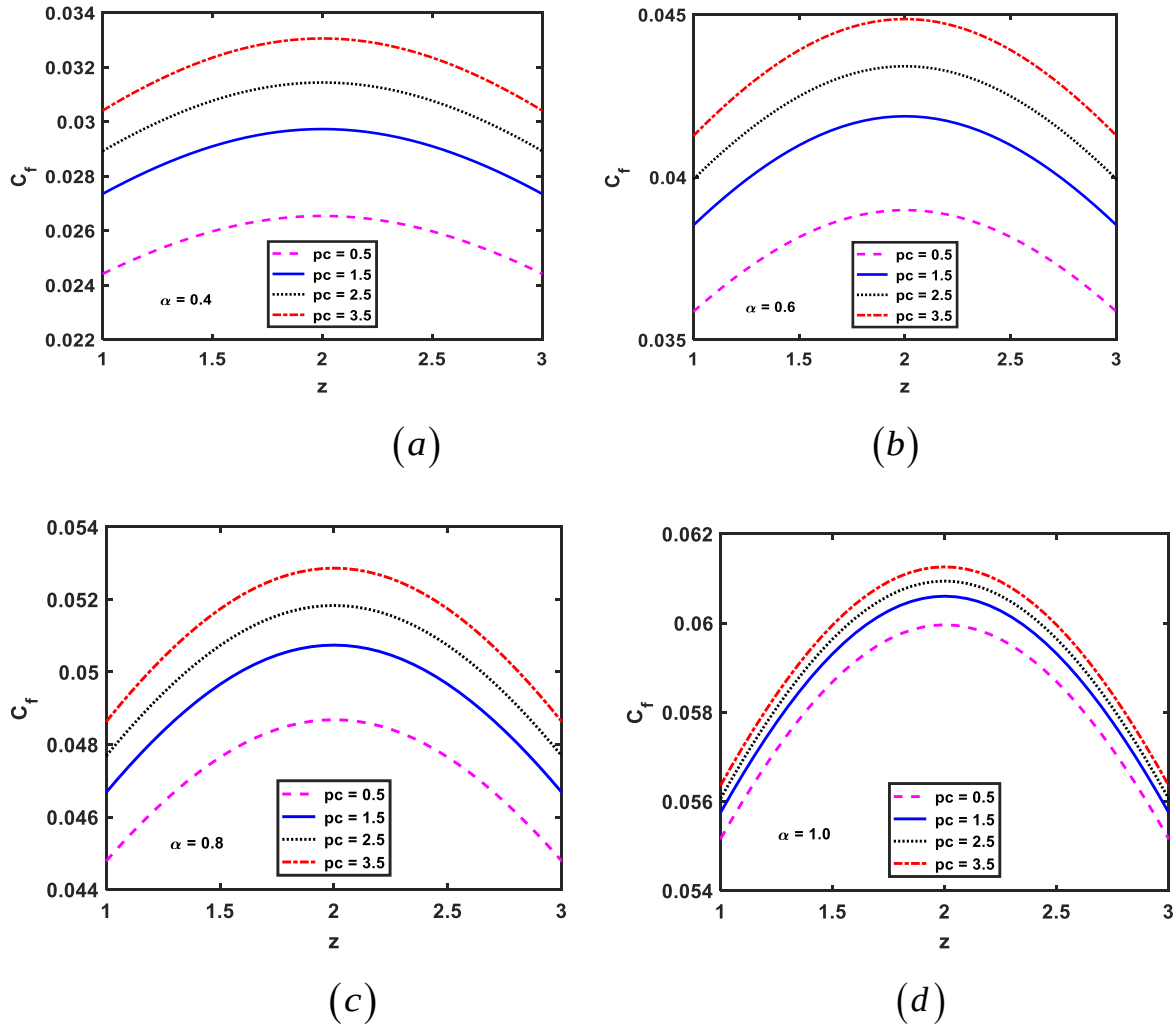


Figure 6.13 Profile of skin friction C_f for different pc with $\lambda_1 = 0.6$, $q_0 = 0.2$, $q_1 = 0.3$, $\ell_0 = 0.8$, $\beta = \pi/6$, $L = 5$, $d = 1$, $L_0 = 2$, $\delta = 0.08$, $t = 0.3$ and $g = 9.81$ when (a) $\alpha = 0.4$, (b) $\alpha = 0.6$, (c) $\alpha = 0.8$, (d) $\alpha = 1.0$.

6.4.6. Conclusion

The findings of the present study are concerned with the flow of blood and the transport of magnetic nanoparticles through an inclined porous artery with mild stenosis under the application of a magnetic field. The Jeffrey fluid represents the rheology of blood flow through the artery. The

magnetic nanoparticles are used as drug delivery applications for atherosclerosis therapy. The governing equations are written in terms of a C-F fractional model and solved using integral transforms. The presence of stenosis significantly impacts the flow of blood, which may be a cause for diseases like heart attacks and strokes. From the present study, the important findings are as follows:

- Increasing the memory effect increases the velocity of blood, the velocity of magnetic nanoparticles, volumetric flow rate, and skin friction.
- The velocity of blood is significantly higher than the velocity of magnetic nanoparticles.
- The volumetric flow rate decreases with elevation in stenosis height. This phenomenon can cause complications in the cardiovascular system, like stroke and heart attack.
- The flow resistance decreases with the enhancement of the memory effect.
- The velocity of blood and velocity of magnetic nanoparticles are boosted with enhancement in the Darcy number and Jeffrey fluid parameter, which shows an important application to the therapy of atherosclerosis.
- The flow resistance increases with an increase in stenosis height and Hartman number.
- The skin friction increases with an increase in magnetic nanoparticles concentration; however, it decreases with an enhancement in stenosis shape and Jeffrey fluid parameters.

The present study is beneficial to the fields of medical science and biomedical engineering in carrying out further research to treat atherosclerosis through nanoparticles based magnetic drug targeting.

7. Conclusions and future scope

In this chapter, various important observations on the trajectory as well as the capture efficacy of drug carrier nanoparticles studied in chapters 4 - 6 are summarized. Further, the future scope of the research related to the capture efficacy of drug carrier nanoparticles during magnetic drug targeting is also described. The details are highlighted below.

7.1. Conclusions

In chapter 4, we focused on the trajectories of drug carrier nanoparticles towards the tumor region in the microvessel during magnetic drug targeting. Various factors that influence the trajectory of drug carrier particles, such as magnetic force, viscous drag force (fluidic force), particle-particle interaction, and Saffman force, are considered. To incorporate the non-local nature of the fluid flow, we introduced the Caputo-Fabrizio time fractional derivative into the momentum equation to provide a better prediction of the trajectories. The velocity of fluid in series form is determined analytically in terms of Bessel functions of the first kind with orders zero and one. The trajectories of drug carrier magnetic nanoparticles and their total volume fraction are obtained numerically using the fourth-order Runge-Kutta (RK-4) method. The controlling parameters such as the particle position, fractional order parameter, magnetization parameter, radius of drug carrier, Darcy number, tumor-magnet distance, Maxwell parameter, Reynolds number, Saffman force parameter, and shape effect have a significant impact on the trajectories of drug carrier magnetic nanoparticles and the total volume fraction of magnetic nanoparticles. An increase in the rheology of blood decreases the capture efficacy of the drug carrier particles. However, the permeability of the vessel that reduces the velocity of carrier particles increases the capture efficacy of the particles near the tumor region. The Saffman uplift force that resists the downward trajectory of the carrier particles reduces the capture efficacy of the particles near the tumor region. Further, larger carrier particles require a smaller volume fraction of drug-carrier magnetic nanoparticles to ensure capture. However, the opposite trend is observed in the case of Darcy number, tumor-magnet distance, Maxwell parameter, Reynolds number, and Saffman force parameter.

In chapter 5, magnetic drug targeting during Casson blood flow from the Caputo time fractional derivative perspective is considered. We used the Laplace transform and Hankel transform of order zero along with their inverse to obtain the analytic solution for the average velocity of fluid. The velocity components of the drug carrier magnetic nanoparticles are calculated using the force balance equation. The effects of biophysical parameters on the radial and axial trajectories of drug carrier particles and on the total volume fraction of magnetic nanoparticles are observed. The analysis demonstrates the impacts of magnetization, Darcy number, Reynolds number, pulsatile frequency, tumor-magnet distance, Casson, and Hematocrit parameters on the capture efficacy of noninvasive magnetic therapy for drugs targeting malignant tissue. The radial trajectories of carrier particles require a higher fractional parameter, magnetization parameter, Darcy number, and Reynolds number for capture near the tumor region; however, the opposite trend is observed during axial trajectories of carrier particles. Total volume fraction of magnetic nanoparticles for capture requires a higher pulsatile frequency, magnetization, Casson, and hematocrit parameters. On the other hand, the total volume fraction of magnetic nanoparticles for capture requires a lower Darcy number, Reynolds number, and tumor magnet distance.

In chapter 6, we focused on the transport of magnetic nanoparticles through an inclined porous artery with mild stenosis. Magnetic nanoparticles are used as an application for the nanoparticle-assisted drug delivery process in blood flow through microvessels to treat cardiovascular disorders that may happen due to atherosclerosis. Atherosclerosis is the thickening or hardening of the arteries, which leads to the blockage of blood flow to other parts of the body and can cause diseases like heart attacks and strokes. In this study, the governing time fractional derivatives are solved using integral transforms. So, the analytic solutions for the velocity of fluid, the velocity of magnetic nanoparticles, skin friction, volume flow rate, and flow resistance are obtained. It is observed that the magnitude of flow velocity of Jeffrey fluid is higher than that of magnetic nanoparticles. Further, the two velocities boost with an increase in memory effect (fractional parameter), Darcy number, and Jeffrey fluid parameter. The volumetric flow rate represents the volume of fluid that passes through a particular region of the vessel per unit of time. It is a function of the velocity of blood and cross-sectional area of the microvessel. Hence, a thorough understanding of volumetric flow rate distribution in the stenosis region is essential to understand complications in the cardiovascular disorder. It is of interest to mention that the volumetric flow

rate decreases with an increase in stenosis height. The flow resistance is one of the important physiological flow variables that affects the blood flow in the stenosis region. It is observed that the flow resistance increases with increasing of stenosis height and Hartman number; however, it decreases with enhancing of the fractional parameter. The fluid flow tangential to the artery's inner wall creates wall shear stress, which causes skin friction. Skin friction is consistent for laminar fluid flow and without artery deformation. However, skin friction may have a major impact on the artery wall because of differences in wall thickness or the existence of stenosis. It is seen that the skin friction is found to be increased with increased magnetic nanoparticles concentration; however, it decreases with increased stenosis shape and Jeffery fluid parameters.

The present study sheds some light on the applications of magnetic drug targeting under controlled release. Unlike drug targeting, some potential applications of the present work include desalination of water and separation of mixtures using applied magnetic field. Applied magnetic field plays a vital role in desalination processes, particularly by weakening bonds between salt ions and water molecules, improving ion separation [266]. Further, Tauo, et al. [267] demonstrated the effectiveness of magnetic field in separating magnetic particles from liquids by attracting and capturing them, a process known as magnetic separation. Magnetic separation is useful in various industries like food processing, recycling, and water treatment. Furthermore, nanoparticles have various applications including separation and purification of biological molecules [261].

7.2. Future scope

In this thesis, we used the semi-analytic approach method to examine the trajectory and capture efficiency of drug carrier nanoparticles near a diseased region during magnetic drug targeting in axisymmetric and stenosed microvessels. One can extend the present investigation by considering the following:

- The time fractional derivative models of non-Newtonian fluids (Maxwell, Casson, and Jeffery fluid models) representing the rheology of blood are considered a single-phase flow nature. Further, researchers may consider the two-phase model in the future. due to the

presence of the glycocalyx layer with peripheral region, the flow nature of the blood follows a two-phase fluid model.

- In general, the dynamic viscosity of fluids is considered constant. However, due to the temperature variation, presence of nanoparticles and the variation of the radius of the microvessel, the viscosity of the blood significantly change which may be considered as future scope.
- The flow of fluid is considered with no slip condition; interested researchers can employ a slip boundary condition for the flow field for further investigations.
- The capture efficacy of drug carrier magnetic nanoparticles during magnetic drug targeting is considered. Researchers may consider tumor immunotherapy mechanisms for the treatment of the tumor with magnetic controlled drug targeting phenomena.
- The nature of blood vessel is not always straight cylindrical shape. Researchers may consider curved artery and bifurcated artery in future.

Bibliography

- [1] A. Malik, T. Tahir Butt, S. Zahid, F. Zahid, S. Waquar, M. Rasool, M. H. Qazi, A. M. Qazi, Use of magnetic nanoparticles as targeted therapy: theranostic approach to treat and diagnose cancer. *J. Nanotechnol.* 2017(2017), 1098765.
- [2] H. Sung, J. Ferlay, R. L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, F. Bray, Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, *CA Cancer J. Clin.* 71(3) (2021) 209-249.
- [3] A. R. Omran, The epidemiologic transition: A theory of the epidemiology of population change. *Milbank Mem Fund Q.* 49(4) (1971) 509-38.
- [4] O. Gersten, J. R. Wilmoth, The cancer transition in Japan since 1951, *Demogr Res.* 7 (2002) 271-306.
- [5] S. Dürr, C. Janko, S. Lyer, P. Tripal, M. Schwarz, J. Zaloga, R. Tietze, C. Alexiou, Magnetic nanoparticles for cancer therapy. *Nanotechnology Reviews*, 2(4) (2013) 395-409.
- [6] S. V. Mathan, M. Rajput, R. P. Singh, Chemotherapy and radiation therapy for cancer, in: B. Jain, S. Pandey (Eds.), *Understanding Cancer*, Academic Press, 2022, PP. 217-236.
- [7] Y.H. Bae, Drug targeting and tumor heterogeneity. *J. Control. Release.* 133(1) (2009) 2–3.
- [8] X. Gao, Y. Cui, R. M. Levenson, L. W. K. Chung, S. Nie, In vivo cancer targeting and imaging with semiconductor quantum dots, *Nat. Biotechnol.* 22 (2004) 969–976.
- [9] S. Bae, K. Ma, T. H. Kim, E. S. Lee, K. T. Oh, E-S. Park, K. C. Lee, Y. S. Youn, Doxorubicin-loaded human serum albumin nanoparticles surface-modified with TNF-related apoptosis-inducing ligand and transferrin for targeting multiple tumor types, *Biomaterials* 33(5) (2012) 1536–1546.
- [10] M. De Palma, M. A. Venneri, C. Roca, L. Naldini, Targeting exogenous genes to tumor angiogenesis by transplantation of genetically modified hematopoietic stem cells, *Nat. Med.* 9 (6) (2003) 789 - 795.
- [11] P.N. Navya, A. Kaphle, H.K. Daima, Nanomedicine in sensing, delivery, imaging and tissue engineering: advances, opportunities and challenges, *Nanoscience* 5 (2019) 30–56.

- [12] R.A. Revia, M. Zhang, Magnetite nanoparticles for cancer diagnosis, treatment, and treatment monitoring: recent advances, *Mater. Today* 19(3) (2016) 157–168.
- [13] A. Bajaj, O. R. Miranda, I-B, Kim, V. M. Rotello, Detection and differentiation of normal, cancerous, and metastatic cells using nanoparticle-polymer sensor arrays. *Proc. Natl. Acad. Sci.* 106(27) (2009) 10912-10916.
- [14] R. Awasthi, A. Roseblade, P. M. Hansbro, M. J. Rathbone, K. Dua, M. Bebawy, Nanoparticles in cancer treatment: Opportunities and obstacles, *Curr. Drug Targets*, 19(14) (2018) 1696-1709.
- [15] M. T. Iqbal, K. Halasz, D. Bhatia, Metallic nanoparticles for targeted drug delivery, *Nanomat. Chem. Tech.* 1 (2017) 3-5.
- [16] F. Watson, P. Austin, Physiology of human fluid balance, *Anaesth. Intensive Care Med.* 22 (2021) 644–651.
- [17] S. Dimmeler, Cardiovascular disease review series. *EMBO Mol. Med.* 3 (2011) 697.
- [18] G. Roth, C. Johnson, A. Abajobir, Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015, *J Am Coll Cardiol.* 70 (1) (2017) 1–25.
- [19] W. Frąk, A. Wojtasińska, W. Lisińska, E. Młynarska, B. Franczyk, J. Rysz. Pathophysiology of Cardiovascular Diseases: New Insights into Molecular Mechanisms of Atherosclerosis, Arterial Hypertension, and Coronary Artery Disease, *Biomedicines*. 10 (8) (2022) 1938.
- [20] N. D. Wong, M. J. Budoff, K. Ferdinand, I. M. Graham, E. D. Michos, T. Reddy, M. D. Shapiro, P. P. Toth, Atherosclerotic cardiovascular disease risk assessment: An American Society for Preventive Cardiology clinical practice statement. *Am J Prev Cardiol.* 10 (2022) 100335.
- [21] R. Ross, Cell biology of atherosclerosis. *Annu Rev Physiol* 57 (1995) 791-804.
- [22] F. A. Scannapieco, R. B. Bush, S. Paju, Associations between periodontal disease and risk for atherosclerosis, cardiovascular disease, and stroke, A systematic review. *Annals of Periodontology* 8(1) (2003) 38-53.
- [23] T. F. Rehring, B. G. Sandhoff, R. S. Stolcpart, J. A. Merenich, H. W. Hollis, Atherosclerotic risk factor control in patients with peripheral arterial disease. *J Vasc Surg.* 41 (2005) 816–822.

- [24] A. H. Gershlick, Treating atherosclerosis: local drug delivery from laboratory studies to clinical trials. *Atherosclerosis*. 160 (2002) 259–271.
- [25] S. Shaw, P. V. S. N. Murthy, P. Sibanda, Magnetic drug targeting in a permeable microvessel, *Microvasc. Res.* 85 (2013), 77-85.
- [26] C. Alexiou, G. Doukas, M. Oc, B. Oc, J. Swaneveldt, N.J. Samani, T.J. Spath, The effect of preoperative atrial fibrillation on survival following mitral valve repair for degenerative mitral regurgitation, *Eur. J. Cardio-Thorac. Surg.* 31 (4) (2007) 586–591.
- [27] E. Falk, Pathogenesis of atherosclerosis, *J. Am. Coll. Cardiol.* 47 (8) (2006) C7–C12.
- [28] M. Cooley, A. Sarode, M. Moore, D.A. Fedosov, S. Mitragotri, A.S. Gupta, Influence of particle size and shape on their margination and wall-adhesion: implications in drug delivery vehicle design across nano-to-micro scale, *Nanoscale*. 10 (2018) 15350–15364.
- [29] M. Enayati, Z. Ahmed, E. Stride, M. Edirisinghe, Preparation of polymeric carriers for drug delivery with different shape and size using an electric jet, *Curr. Pharm. Biotechnol.* 10 (2009) 600–608.
- [30] D. Canelas, K.P. Herlitz, J.M. DeSimone, Top-down particle fabrication: control of size and shape for diagnostic imaging and drug delivery, *Wiley Interdiscip. Rev. Nanomed. Nanobiotechnol.* 1 (2009) 391–404.
- [31] N. Doshi, S. Mitragotri, Designer biomaterials for nanomedicine, *Adv. Mater.* 19 (2009) 3843–3854.
- [32] A. Yamamoto, R. Honma, M. Sumita, T. Hanawa, Cytotoxicity evaluation of ceramic particles of different sizes and shapes, *J. Biomed. Mater. Res. Part A* 68A (2) (2004) 244–256.
- [33] J.A. Champion, Y.K. Katare, S. Mitragotri, Particle shape: a new design parameter for micro-and nanoscale drug delivery carriers, *J. Control. Release* 121 (2007) 3–9.
- [34] [34] J.A. Champion, S. Mitragotri, Role of target geometry in phagocytosis, *Proc. Natl. Acad. Sci.* 103 (2006) 4930–4934.
- [35] R. Dinc, Magnetic nanoparticles with aspects of their use in cancer therapy, *Lett. Drug. Des. Discov.* 21 (2024) 847-857.
- [36] P. Dehghankelishadi, M. F. Maritz, N. Dmochowska, P. Badiie, E. Cheah, I. Kempson, R. I. Berbeco, Thierry B. Formulation of simvastatin within high density lipoprotein enables potent tumour radiosensitisation, *J. Control. Release*. 346 (2022) 98-109.

- [37] T. Ashutosh, A. Tiwari, Nanomaterials in drug delivery, imaging, and tissue engineering. John Wiley & Sons, 2013.
- [38] R. Rasheed, V. Meera, Synthesis of iron oxide nanoparticles coated sand by biological method and chemical method. *Proc. Technol.* 24 (2016) 210-216.
- [39] A. Nyabadza, E. McCarthy, M. Makhesana, S. Heidarinasab, A. Plouze, M. Vazquez, D. Brabazon, A review of physical, chemical and biological synthesis methods of bimetallic nanoparticles and applications in sensing, water treatment, biomedicine, catalysis and hydrogen storage. *Adv. Colloid Interface Sci.* 321 (2023) 103010.
- [40] D. Amara, I. Felner, I. Nowik, S. Margel, Synthesis and characterization of Fe and Fe₃O₄ nanoparticles by thermal decomposition of triiron dodecacarbonyl, *Colloids Surf. A: Physicochem. Eng.*, 339 (2009), 106-110.
- [41] C. Li, Y. Wei, A. Liivat, Y. Zhu, J. Zhu, Microwave-solvothermal synthesis of Fe₃O₄ magnetic nanoparticles. *Mater. Lett.* 107 (2013) 23-26.
- [42] C. Solans, P. Izquierdo, J. Nolla, N. Azemar, M. J. Garcia-Celma, Nano-emulsions, *Curr. Opin. Colloid Interface Sci.* 10 (2005) 102-110.
- [43] A. B. Chin, I. I. Yaacob, Synthesis and characterization of magnetic iron oxide nanoparticles via w/o microemulsion and Massart's procedure. *J. Mater. Process. Technol.* 191 (2007) 235-237.
- [44] K. N. Thakkar, S. S. Mhatre, R. Y. Parikh, Biological synthesis of metallic nanoparticles. *Nanomedicine*, 6(2) (2010) 257-262.
- [45] L. Euler, *Mémoires de l'Académie des Sciences*, Berlin, 11 (1757).
- [46] [46]C.L. Navier, *Annales de Chimie et de Physique*, 19 (1821).
- [47] C.L. Navier, *Mémoires de L'Académie Royale des Sciences de L'Institut de France*, 6 (1827).
- [48] G. G. Stokes, On the Theories of the Internal Friction of Fluids in Motion and of the Equilibrium and Motion of Elastic Solids. *Trans. Cambridge Philos. Soc.*, 8 (1845) 287-319.
- [49] O. Darrigol, Between Hydrodynamics and Elasticity Theory: The First Five Births of the Navier- Stokes Equation, *Arch. Hist. Exact Sci.*, 56(2) (2002): pp. 95-150.
- [50] S. R. Bistafa, On the development of the Navier-Stokes equation by Navier. *Revista Brasileira de Ensino de Física*, 40(2) (2018), e2603.

- [51] B. K. Sultanian, Fluid mechanics: An intermediate approach, CRC press, 2015.
- [52] R. G. Owens, T. N. Phillips, Computational Rheology; Imperial College Press: London, 2002.
- [53] R. G. M. Van Os, T. N. Phillips, Spectral element methods for transient viscoelastic flow problems, J. Comput. Phys. 2001 (2004) 286–314.
- [54] A. F. Morais, H. Seybold, H. J. Herrmann, J. S. Andrade, Non-Newtonian Fluid Flow through Three-Dimensional Disordered Porous Media, J. Phys Rev. Lett. 103 (2009) 194502.
- [55] T. Sochi, Flow of non-Newtonian fluids in porous media. J. Polym. Sci., Part B: Polym. Phys. 48(23) (2010) 2437-2767.
- [56] R. P. Chhabra, J. F. Richardson, Non-Newtonian Flow in the Process Industries; Butterworth Heinemann Publishers, Oxford, 1999.
- [57] D. Alghalibi, Numerical study of particle suspensions in Newtonian and non-Newtonian fluids (Doctoral dissertation, KTH Royal Institute of Technology), 2019.
- [58] F. Morrison, Understanding Rheology, 1st ed., Oxford University Press, Inc., New York, 2001.
- [59] L. Dean, Blood and the cells it contains, in: Blood Groups Red Cell Antigens, National Center for Biotechnology Information, 2005: pp. 1–6.
- [60] C. Tu, M. Deville, Pulsatile flow of non-newtonian fluids through arterial stenoses, J. Biomech. 29 (7) (1996) 899–908.
- [61] P. K. Kundu, I. M. Cohen, D. R. Dowling, Fluid Mechanics. Academic Press, San Diego, 2016.
- [62] N. Casson, A Flow Equation for Pigment-Oil Suspensions of the Printing Ink Type. In: Mill, C.C., Ed., Rheology of Disperse Systems, Pergamon Press, Oxford, (1959) 84-104.
- [63] M. Reiner, G. W. Scott Blair, The flow of blood through narrow tubes. Nature, 184 (4683) (1959) 354-354.
- [64] S. Chien, R. G. King, R. Skalak, S. Usami, A. L. Copley, Viscoelastic properties of human blood and red cell suspensions, Biorheology 12 (1975) 341–346).
- [65] G. B. Thurston, Viscoelasticity of human blood, Biophys J. 12(9) (1972) 1205-17.
- [66] G. B. Thurston, Frequency and shear rate dependence of viscoelasticity of human blood. Biorheology. 10(3) (1973) 375-81.

- [67] C. Fetecau, M. Athar, C. Fetecau, Unsteady flow of a generalized Maxwell fluid with fractional derivative due to a constantly accelerating plate, *Comput. Math. Appl*, 57(4) (2009) 596-603.
- [68] T. Hayat, N. Ahmad, N. Ali, Effects of an endoscope and magnetic field on the peristalsis involving Jeffrey fluid. *Communications in Nonlinear Science and Numerical Simulation*, 13(8) (2008) 1581-1591.
- [69] I. L. Animasaun, E. A. Adebile, A. I. Fagbade, Casson fluid flow with variable thermo-physical property along exponentially stretching sheet with suction and exponentially decaying internal heat generation using the homotopy analysis method. *J. Nigerian Math. Soc.* 35(1) (2016) 1-17.
- [70] F. Shaikh, A. A. Shaikh, E. Hincal, S. Qureshi, Comparative analysis of numerical simulations of blood flow through the segment of an artery in the presence of stenosis. *J. Appl. Math. Comput. Mech*, 22(2) (2023), pp.49-61.
- [71] Yu-Shu Wu, *Flow-Governing Equations and Mathematical Models*, Editor(s): Yu-Shu Wu, *Multiphase Fluid Flow in Porous and Fractured Reservoirs*, Gulf Professional Publishing, (2016) 29-47.
- [72] R. R. Vasiljevic, R.R., 2023. Numerical methods and their application in dynamics of structures. *Vojnotehnički glasnik/Military Technical Courier*, 71 (2023) 452-472.
- [73] E. Grunschloss, *Polymer, Single Screw Extrusion: Modeling*, Editor(s): K.H. Jurgen Buschow, R. W. Cahn, M. C. Flemings, B. Ilshner, E. J. Kramer, S. Mahajan, P. Veyssiere, *Encyclopedia of Materials: Science and Technology*, (2001) 7491-7504
- [74] M. E. García, *Bessel functions and equations of mathematical physics*, 2016.
- [75] S. Das, *Functional fractional calculus*, Berlin: Springer; 2011.
- [76] T. T. Hartley, C. F. Lorenzo, *The Vector Linear Fractional Initialization Problem*, NASA/TP-1999-208919, 1999.
- [77] R. B'elohl'avek, *Fuzzy Relational Systems: Foundations and Principles*, Kluwer Academic Publishers, New York, 2002.
- [78] F. Tenoudji, *Analog and Digital Signal Analysis: From Basics to Applications*, Springer, Switzerland, 2016.
- [79] A. M. Yaglom, *An Introduction to the Theory of Stationary Random Functions*. Revised English edn. Translated and edited by Richard A. Silverman, vol. XIII. Prentice-Hall, Inc., Englewood Cliffs (1962).

- [80] P. P. G. Dyke, P. P Dyke, An introduction to Laplace transforms and Fourier series, Springer, London, 2001.
- [81] J. L. Schiff, The Laplace transform: theory and applications. Springer Science & Business Media, 2013.
- [82] L. Debnath, D. Bhatta, Integral transforms and their applications, Chapman and Hall/CRC, 2016.
- [83] A. D. Poularikas, A. M. Grigoryan, Transforms and applications handbook, CRC press, 2018.
- [84] B. Zheng, (G'/G) -expansion method for solving fractional partial differential equations in the theory of mathematical physics. Commun. Theor. Phys. 58 (2012) 623–630.
- [85] D. Tavares, R. Almeida, D.F.M. Torres, Caputo derivatives of fractional variable order: numerical approximations. Commun. Nonlinear Sci. Numer. Simul. 35 (2016) 69–87.
- [86] J. Liouville, Mémoire sur le calcul des différentielles à indices quelconques, J. l'Ecole Roy. Polytechn. 13 (1832) 71–162.
- [87] D.S. Grebenkov, M. Vahabi, E. Bertseva, L. Forró, S. Jeney, Hydrodynamic and subdiffusive motion of tracers in a viscoelastic medium, Phys. Rev. E. 88 (2013) 040701.
- [88] A.V. Letnikov, Theory of differentiation with an arbitrary index (Russian). Moscow Matem. Sbornik. 3 (1868) 1–66.
- [89] H. Laurent, Sur le calcul des dérivées à indices quelconques. Nouvelles Annales de Mathématiques 3(1884) 240–252.
- [90] H. Weyl, Bemerkungen zum Begriff des differential quotienten gebrochener Ordnung, Vierteljschr. Naturforsch. Gesellsch, Zürich. 62 (2017) 296–302.
- [91] M. Riesz, L'intégrales de Riemann-Liouville et le problème de Cauchy, Acta Math. 81 (1949) 1–223.
- [92] R. Hilfer, Applications of Fractional Calculus in Physics, World scientific, Singapore 2000.
- [93] A.A. Kilbas, H.M. Srivastava, J.J. Trujillo, Theory and Applications of Fractional Differential Equations, Elsevier, Netherlands, 2006.
- [94] I. Podlubny, Fractional Differential Equations, Academic Press, San Diego, 1999.
- [95] S. Samko, A. Kilbas, O. Marichev, Fractional Integrals and derivatives: Theory and Applications, Gordon and Breach, Amsterdam, 1993.

- [96] J. Cresson, Fractional embedding of differential operators and Lagrangian systems. *J. Math. Phys.* 48 (2007) 033504.
- [97] O.P. Agrawal, Generalized variational problems and Euler-Lagrange equations. *Comput. Math. Appl.* 59 (2010) 1852–1864.
- [98] L. Bourdin, T. Odziejewicz, D.F.M. Torres, Existence of minimizers for generalized Lagrangian functionals and a necessary optimality condition-application to fractional variational problems. *Differ. Integral. Equ.* 27 (2014) 743–766.
- [99] M. Caputo, Linear models of dissipation whose Q is almost frequency independent II, *Geophys. J. Royal Astron. Soc.* 13 (1967) 529–539.
- [100] M. Caputo, *Elasticita e Dissipazione*, Zanichelli, Bologna, 1969.
- [101] R. L. Bagley, P. J. Torvik, On the fractional calculus model of viscoelastic behavior, *J. Rheol.* 30 (1986) 133–155.
- [102] M. Caputo and F. Mainardi, A new dissipation model based on memory mechanism, *Pure Appl. Geophys.* 91 (1971) 134–147.
- [103] M. Caputo, M. Fabrizio, A New Definition of Fractional Derivative without Singular Kernel, *Progr. Fract. Differ. Appl.* 1(2) (2015) 1-13.
- [104] T. Anjum, N. Hussain, Hafsa, H.M.N. Iqbal, A, Jedrzak, T. Jesionowski, M. Billai, Magnetic nanomaterials as drug delivery vehicles and therapeutic constructs to treat cancer, *J Drug Deliv Sci Technol.* 80 (2023) 104103.
- [105] R. Ellahi, The effects of MHD and temperature dependent viscosity on the flow of non-Newtonian nanofluid in a pipe: Analytical solutions, *Applied Mathematical Modelling* 37 (2013) 1451–1467.
- [106] N. S. Elgazery, A. F. Elelmy, E. Bobescu, R. Ellahi, How do artificial bacteria behave in magnetized nanofluid with variable thermal conductivity: application of tumor reduction and cancer cells destruction, *Methods for Heat & Fluid Flow*, 32 (2022) 2982-3006.
- [107] M.M. Bhatti, A. Zeeshan, R. Ellahi, O. Anwar Bég, A. Kadir, Effects of coagulation on the two-phase peristaltic pumping of magnetized Prandtl biofluid through an endoscopic annular geometry containing a porous medium, *Chinese Journal of Physics* 58 (2019) 222–234.

- [108] M. A. Yousif, H. F. Ismael, T. Abbas, R. Ellahi, Numerical study of momentum and heat transfer of MHD Carreau nanofluid over an exponentially stretched plate with internal heat source/sink and radiation, *Heat Transfer Research*, 50 (2019) 649-658.
- [109] H. Aslam, S. Shukrullah, M.Y. Naz, H. Fatima, H. Hussain, S. Ullah, M.A. Assiri, Current and future perspectives of multifunctional magneti nanoparticles based controlled drug delivery systems, *J Drug Deliv Sci Technol*, 67 (2022) 102946.
- [110] M. Mahmoodpour, M. Goharkhah, M. Ashjaee, M. Najafi, A three-dimensional numerical investigation on trajectories and capture on magnetic drug carrier nanoparticles in a Y-shaped vessel, *J Drug Deliv Sci Technol*. 61 (2021) 102207.
- [111] M. Cooley, A. Sarode, M. Moore, D. A. Fedosov, S. Mitragotri, A. S. Gupta, Influence of particle size and shape on their margination and wall-adhesion: implications in drug delivery vehicle design across nano-to-micro scale, *Nanoscale* 10 (2018) 15350-15364.
- [112] J. A. Champion, Y. K. Katare, S. Mitragotri, Particle shape: A new design parameter for micro-and nanoscale drug delivery carriers, *J. Control. Release* 121 (2007) 3 – 9.
- [113] J. A. Champion, S. Mitragotri, Role of target geometry in phagocytosis, *PNAS* 103 (2006) 4930-4934.
- [114] D. Tripathi, J. Prakash, A. K. Tiwari, R. Ellahi, Thermal, microrotation, electromagnetic field and nanoparticle shape effects on Cu-CuO/blood flow in microvascular vessels, *Microvascular Research* 132 (2020) 104065.
- [115] M. M. Bhatti, S. M. Sait, R. Ellahi, Magnetic Nanoparticles for Drug Delivery through Tapered Stenosed Artery with Blood Based Non-Newtonian Fluid, *Pharmaceuticals*, 15 (2022) 1352.
- [116] P. Decuzzi, R. Pasqualini, W. Arap, M. Ferrari, Intravascular Delivery of Particulate Systems: Does Geometry Really Matter?. *Pharm Res* 26 (2009) 235–243.
- [117] J.H Park, G. von Maltzahn, L. Zhang, M. P. Schwartz, E. Ruoslahti, S. N. Bhatia, M. J. Saito, Magnetic Iron Oxide Nanoworms for Tumor Targeting and Imaging. *Adv. Mater.* 20 (2008)1630-1635.
- [118] D. Vieru, C. Fetecau, Flow of a viscoelastic fluid with the fractional Maxwell model between two side walls perpendicular to a plate, *Appl. Math. Comput.* 200 (2008) 459–464.

- [119] Y. Mahsud, N. A. Shah, D. Vieru, Influence of time-fractional derivatives on the boundary layer flow of Maxwell fluids, *Chinese J. Phys.* 55 (2017) 1340–1351.
- [120] C. Li, L. Zheng, X. Zhang, G. Chen, Flow and heat transfer of a generalized Maxwell fluid with modified fractional Fourier's law and Darcy's law, *Comput Fluids* 125 (2016) 25–38.
- [121] M. Shen, S. Chena, F. Liu, Unsteady MHD flow and heat transfer of fractional Maxwell viscoelastic nanofluid with Cattaneo heat flux and different particle shapes, *Chinese J. Phys.* 56 (2018) 1199-1211.
- [122] S. Wang, M. Zhao, Analytical solution of the transient electro-osmotic flow of a generalized fractional Maxwell fluid in a straight pipe with a circular cross-section, *Eur J Mech B Fluids* 54 (2015) 82–86
- [123] N. A. Shah, D. Vieru, C. Fetecau, Effects of the fractional order and magnetic field on the blood flow in cylindrical domains, *J. Magn. Magn. Mater.* 409 (2016) 10-19.
- [124] F. Ali, N. A. Sheikh, I. Khan, M. Saqib, Magnetic field effect on blood flow of Casson fluid in axisymmetric cylindrical tube: A fractional model, *J. Magn. Magn. Mater.* 423(2017), 327-336.
- [125] D. F. Jamil, S. Saleem, R. Roslan, F. S. Al-Mubaddel, M. Rahimi-Gorji, A. Issakhov, S. U. Din, Analysis of non-Newtonian magnetic Casson blood flow in an inclined stenosed artery using Caputo-Fabrizio fractional derivatives, *Comput. Methods Programs Biomed.* 203 (2021) 106044.
- [126] C.D.K. Bansi, C.B. Tabi, T.G. Motsumi, A. Mohamadou, Fractional blood flow in oscillatory arteries with thermal radiation and magnetic field effects, *J. Magn. Magn. Mater.* 456 (2018), 38-45.
- [127] H. B. Yadeta, S. Shaw, Magnetic drug targeting during Casson blood flow in a microvessel: A Caputo fractional model, *J. Magn. Magn. Mater.* 568 (2023) 170363.
- [128] S. Maiti, S. Shaw, G.C. Shit, Fractional order model for thermochemical flow of blood with Dufour and Soret effects under magnetic and vibration environment, *Colloids Surf. B* 197 (2021) 111395.
- [129] S. Maiti, S. Shaw, G.C. Shit, Fractional order model of thermo-solutal and magnetic nanoparticles transport for drug delivery applications, *Colloids Surf. B* 203 (2021) 111754.

- [130] S. Shaw, S. Ganguly, P. Sibanda, S. Chakraborty, Dispersion characteristics of blood during nanoparticle assisted drug delivery process through a permeable microvessel, *Microvasc. Res.* 92 (2014) 25-33.
- [131] S. Majeed, F. Ali, A. Imtiaz, I. Khan, M. Andualet, Fractional model of MHD blood flow in a cylindrical tube containing magnetic particles. *Sci. Rep.* 12 (2022) 418.
- [132] Y. Bai, Y. Jiang, F. Liu, Y. Zhang, Numerical analysis of fractional MHD Maxwell fluid with the effects of convection heat transfer condition and viscous dissipation, *AIP Advances* 7 (2017) 125309.
- [133] Y. Zhang, J. Gao, Y. Bai, Q. Wang, D. Sun, X. Sun, B. Lv, Numerical simulation of the fractional Maxwell fluid flow in locally narrow artery, *Computer Methods in Biomechanics and Biomedical Engineering* 26, no. 11 (2023)1272-1287.
- [134] R. Tang, S. Rehman, A. Farooq, M. Kamran, M. I. Qureshi, A. Fahad, J.-B. Liu, A comparative study of natural convection flow of fractional Maxwell fluid with uniform heat flux and radiation, *Complexity* 2021 (2021) 9401655.
- [135] M. A. El Kot, Y. A. Elmaboud, Unsteady pulsatile fractional Maxwell viscoelastic blood flow with Cattaneo heat flux through a vertical stenosed artery with body acceleration. *J. Therm. Anal. Calorim.* 147 (2022) 4355–4368.
- [136] A. Riaz, E. Bobescu, K. Ramesh, R. Ellahi, Entropy Analysis for Cilia-Generated Motion of Cu-Blood Flow of Nanofluid in an Annulus, *Symmetry*, 18 (2021) 2358.
- [137] A. U. Rehman, M. B. Riaz, A. Atangana, Fahd Jarad, J. Awrejcewicz, Thermal and concentration diffusion impacts on MHD Maxwell fluid: A generalized Fourier's and Fick's perspective, *Case Stud. Therm. Eng.* 35 (2022) 102103.
- [138] S. Aman, Q. Al-Mdallal, I. Khan, Heat transfer and second order slip effect on MHD flow of fractional Maxwell fluid in a porous medium, *J. King Saud Univ. Sci.* 32 (2020) 450–458.
- [139] Y. Liu, X. Chi, H. Xu, X. Jiang, Fast method and convergence analysis for the magnetohydrodynamic flow and heat transfer of fractional Maxwell fluid, *Appl. Math. Comput.* 430 (2022) 127255.
- [140] Y. Qiao, X. Wang, H. Xu, H. Qi, Numerical analysis for viscoelastic fluid flow with distributed/variable order time fractional Maxwell constitutive models. *Appl. Math. Mech.-Engl. Ed.* 42 (2021) 1771–1786.

- [141] X. Yang, H. Qi, X. Jiang, Numerical analysis for electroosmotic flow of fractional Maxwell fluids, *Appl. Math. Lett.* 78 (2018) 1-8.
- [142] M. Saqib, H. Hanif, T. A.jawad, I. Khan, S. Shafie, K. S. Nisar, Heat transfer in MHD flow of Maxwell fluid via fractional Cattaneo-Friedrich model: A Finite Difference Approach, *Computers, Materials & Continua* 65 (2020) 1959-1973.
- [143] X. Wang, Y. Qiao, H. Qi, H. Xu, Numerical study of pulsatile non-Newtonian blood flow and heat transfer in small vessels under a magnetic field, *Int. Commun. Heat Mass Transf.* 133 (2022) 105930.
- [144] P.K. Mandal, An unsteady analysis of non-Newtonian blood flow through tapered arteries with a stenosis, *Int. J. Non-Linear Mech.* 40 (2005) 151 – 164.
- [145] T. Şuayip, The Existence and Uniqueness of Initial-Boundary Value Problems of the Fractional Caputo-Fabrizio Differential Equations, *Univers. J. Math. Appl.* 6(2)2019 100-106.
- [146] I. Podlubny. *Fractional differential equations: An introduction to fractional derivatives, fractional differential equations, to methods of their solution and some of their applications*, Elsevier, 1998.
- [147] C. Alonso, A. R. Pries, O. Kiesslich, D. Lerche, P. Gaehtgens, Transient rheological behavior of blood in low-shear tube flow: velocity profiles and effective viscosity, *Am. J. Physiol. Cell Physiol.* 268 (1995) H25-H32.
- [148] A. R. Pries, T. W. Secomb, T. Gessner, M. B. Sperandio, J. F. Gross, P. Gaehtgens, Resistance to blood flow in microvessels in vivo. *Circ. Res.* 75 (1994) 904 – 915.
- [149] A.R. Pries, T.W. Secomb, P. Gaehtgens, Biophysical aspects of blood flow in the microvasculature, *Cardiovasc. Res.* 32 (1996) 654 – 667.
- [150] H.C. Brinkman, The viscosity of concentrated suspensions and solutions. *J. Chem. Phys.* 20 (1952) 571–581.
- [151] A. Einstein, A new determination of molecular dimensions. *Ann. Phys.* 19 (1906) 289–306.
- [152] S. Ganguly, S. Chakraborty, Effective viscosity of nanoscale colloidal suspensions, *J. Appl. Phys.* 106 (2009) 124309.

- [153] L. Pasol, F. Feuillebois, Effective viscosity of an inhomogeneous dilute suspension flowing along a wall. XII International Congress of Theoretical and Applied Mechanics, Warsaw, Poland, 15–21 August 2004.
- [154] P. G. Saffman, The lift on a small sphere in a slow shear flow, *J. Fluid Mech.* 22 (1965) 385-400.
- [155] A. Sutradhar, Effects of buoyant and Saffman lift force on magnetic drug targeting in microvessel in the presence of inertia, *Microvasc. Res.* 133 (2021) 104099.
- [156] E. J. Furlani, E. P. Furlani, A model for predicting magnetic targeting of multifunctional particles in microvasculature, *J. Magn. Magn. Mater.* 312 (2007) 187–193.
- [157] M. K. D. Manshadi, M. Saadat, M. Mohammadi, M. Shamsi, M. Dejam, R. Kamali, and A. Sanati-Nezhad. Delivery of magnetic micro/nanoparticles and magnetic-based drug/cargo into arterial flow for targeted therapy. *Drug delivery* 25 (1) (2018) 1963-1973.
- [158] L. R. Mashiku, S. Shaw, Unsteady nano-magnetic drug dispersion for pulsatile Darcy flow through microvessel with drug elimination phenomena, *Phys. Fluids* 35 (2023) 101909.
- [159] C. Crone, The permeability of capillaries in various organs as determined by use of the ‘indicator diffusion’ method, *Acta Physiol. Scand.* 58 (1963) 192–305.
- [160] L. Casanellas, J. Ortín, Laminar oscillatory flow of Maxwell and Oldroyd-B fluids: theoretical analysis, *J. Non-Newtonian Fluid Mech.* 166 (2011) 1315–1326.
- [161] M.M. Larimi, A. Ramiar, A.A. Ranjbar, Numerical simulation of magnetic nanoparticles targeting in a bifurcation vessel. *J. Magn. Magn. Mater.* 362 (2014) 58–71.
- [162] X. Zheng, Z. Silber-Li, The influence of Saffman lift force on nanoparticle concentration distribution near a wall, *Appl. Phys. Lett.* 95 (2009) 124105.
- [163] P. Journey, R. Agarwal, V. Singh, D. Choi, K. Roy, S. L. Shi, Unique size and shape-dependent uptake behaviors of non-spherical nanoparticles by endothelial cells due to a shearing flow, *J. Control Release.* 245 (2017) 170-176.
- [164] S. Nejati, E. M. Vadeghani, S. Khorshidi, A. Karkhane, Role of particle shape on efficient and organ-based drug delivery, *Eur. Polym. J.* 122 (2020) 109353.
- [165] S. Khorshidi, A. Karkhaneh, S. Bonakdar, Fabrication of amine-decorated nonspherical microparticles with calcium peroxide cargo for controlled release of oxygen, *J. Biomed. Mater. Res. Part A* 108 (2019) 136-147.

- [166] W. Li, T. Suzuki, H. Minami, The interface adsorption behavior in a Pickering emulsion stabilized by cylindrical polystyrene particles, *J. Colloid Interface Sci.* 552 (2019) 230–235.
- [167] S. E. A. Gratton, P. A. Ropp, P. D. Pohlhaus, J. C. Luft, V. J. Madden, M. E. Napier, and J. M. DeSimone, The effect of particle design on cellular internalization pathways. *Proceedings of the National Academy of Sciences* 105, no. 33 (2008): 11613-11618.
- [168] J. Cao, J-S. Choi, M. A. Oshi, J. Lee, N. Hasan, J. Kim, J-W. Yoo, Development of PLGA micro- and nanorods with high capacity of surface ligand conjugation for enhanced targeted delivery, *Asian J. Pharm. Sci.* 14 (1) (2019) 86–94.
- [169] E. A. Simone, T. D. Dziubla, V. R. Muzykantov, Polymeric carriers: role of geometry in drug delivery, *Expert Opin. Drug Deliv.* 5 (2008) 1283 – 1300.
- [170] A. Srivastav, B. Chandanshive, P. Dandekar, D. Khushalani, R. Jain, Biomimetic hydroxyapatite a potential universal nanocarrier for cellular internalization & drug delivery, *Pharm. Res.* 36 (4) (2019) 60.
- [171] R. Bali, N. Gupta, S. Mishra, Dispersion characteristics of non-Newtonian fluid during transportation of nanoparticles in permeable capillary, *Appl. Appl. Math.* 11(2) (2016) 632–645.
- [172] C. Alexiou, R. Tietze, E. Schreiber, R. Jurgons, H. Richter, L. Trhams, H. Rahn, S. Odenbach, S. Lyer, Cancer therapy with drug loaded magnetic nanoparticles - magnetic drug targeting, *J. Magn. Magn. Mater.* 323 (2011) 1404–1407.
- [173] J. P. Ndenda, S. Shaw, J. B.H. Njagarah, Solute dispersion of drug carrier during magnetic drug targeting for blood flow through a microvessel, *J. Appl. Phys.* 130 (2021) 024701.
- [174] E.J. Furlani, K.C. Ng, Analytical model of magnetic nanoparticle transport and capture in the microvasculature, *Phys. Rev. E* 73, 061919 (2006).
- [175] A. Sutradhar, P. V. S. N. Murthy, and S. Shaw, Magnetic drug targeting in an impermeable microvessel with the influence of inertia of multifunctional carrier particle, *J. Nanofluids* 5 (2016) 728–735.
- [176] S. Bose, M. Banerjee, Effect of non-Newtonian characteristics of blood on magnetic particle capture in occluded blood vessel, *J. Magn. Magn. Mater.* 374 (2015) 611–623.

- [177] S. Shaw, P.V.S.N., Murthy, S. C. Pradhan, Effect of non-Newtonian characteristics of blood on magnetic targeting in the impermeable micro-vessel, *J. Magn. Magn. Mater.* 322 (2010) 1037–1043.
- [178] M. Mahmoodpour, M. Goharkhah, M. Ashjaee, Investigation on trajectories and capture of magnetic drug carrier nanoparticles after injection into a direct vessel, *J. Magn. Magn. Mater.* 497 (2020) 166065.
- [179] S. Shaw, A. Sutradhar, P. V.S.N. Murthy, Permeability and stress-jump effects on magnetic drug targeting in a permeable microvessel using darcy model, *J. Magn. Magn. Mater.* 429 (2017) 227–235.
- [180] N. Choomphon-anomakhun, A. D. Ebner, M. Natenapit, J.A. Ritter, Simulation of dynamic magnetic particle capture and accumulation around a ferromagnetic wire, *J. Magn. Magn. Mater.* 428 (2017) 493–505.
- [181] A. A. Zafar, N. A. Shah, I. Khan, Two phase flow of blood through a circular tube with magnetic properties, *J. Magn. Magn. Mater.* 477 (2017) 382–387.
- [182] P. Sibanda, S. Shaw, A model for magnetic drug targeting in a permeable microvessel with spherical porous carrier particles, in: *Proceedings of the 5th Inter. Conf. on Porous Media and its Applications in Science and Engineering*, (2014).
- [183] A. D. Grief, G. Richardson, Mathematical modeling of magnetically targeted drug delivery, *J. Magn. Magn. Mater.* 293 (2005) 455–463.
- [184] C.R. Uthra, R. Vasanthakumari, Mathematical model for nanomagnetic drug delivery and targeting using computational methods, *World Appl. Sci. J.* 34 (8) (2016) 1083–1089.
- [185] S. Majee, and G.C. Shit, Modeling and simulation of blood flow with magnetic nanoparticles as carrier for targeted drug delivery in the stenosed artery, *European Journal of Mechanics / B Fluids* 83 (2020) 42–57.
- [186] A. Ardalan, S. Aminian, A. Seyfaee, S. Gharehkhani, Effects of geometrical parameters on the capture efficiency of nanoparticles under the influence of the magnetic field in a stenosed vessel, *Powder Technol.* 380 (2021) 39–46.
- [187] K. Kakavand, N. Koosha, K. Fathi, S. Aminian, Numerical investigation of capture efficiency of carrier particles in a Y-shaped vessel considering particle-particle interaction and non-Newtonian behavior, *J Drug Deliv Sci Technol* 67 (2022) 102997.

- [188] M. Zandi, M. Zare, H. Nazari, M. Ashjaee, A. A. Zale, Investigating the effect of injection rate on the capture efficiency of nanoparticles in different geometries of stenosed vessel, *J. Magn. Magn. Mater.* 544 (2022) 168665.
- [189] V. P. Rathod, S. Tanveer, Pulsatile flow of couple stress fluid through a porous medium with periodic body acceleration and magnetic field, *Bull. Malays. Math.Sci. Soc.* 32 (2009) 245–259.
- [190] J. Venkatesan D. S. Sankar K. HemalathaY.Yatim, Mathematical analysis of Casson fluid model for blood rheology in stenosed narrow arteries, *J. Appl. Math.*, 2013, pp. 1–11.
- [191] R. Bali, U. Awasthi, A Casson fluid model for multiple stenosed artery in the presence of magnetic field, *AM* 03 (2012) 436–441.
- [192] D. S. Sankar, Two-fluid flow of blood through asymmetric and axisymmetric stenosed narrow arteries, *Int. J. Nonlinear Sci. Numer. Simul.* 10 (2009) 1425-1441.
- [193] E.W. Merrill, A.M. Benis, E.R. Gilliland, T.K. Sherwood, E.W. Salzman, Pressure flow relations of human blood in hollow fibers at low flow rates, *J. Appl. Physiol.* 20 (1965) 954–967.
- [194] T. Hayat, S. Asad, A. Alsaedi, Flow of Casson fluid with nanoparticles, *Appl. Math. Mech.* 37 (2016) 459–470.
- [195] H. I. Osman, D. Vieru, Z. Ismail, Transient axisymmetric flows of Casson Fluids with generalized Cattaneo’s Law over a vertical cylinder, *Symmetry* 14 (2022) 1319.
- [196] F. Ali, F. Haq, N. Khan, A. Imtiaz, I. Khan, A time fractional model of hemodynamic two-phase flow with heat conduction between blood and particles: applications in health science, *Waves in Random and Complex Media*.
- [197] F. Ali, F. Haq, N. Khan, H. Alqahtani, A. Imtiaz, I. Khan, A report of generalized blood flow model with heat conduction between blood and particles, *J. Magn.* 27 (2022) 186-200.
- [198] J. Shah, F. Ali, N. Khan, Z. Ahmad, S. Murtaza, I. Khan, O. Mahmoud, MHD flow of time-fractional Casson nanofluid using generalized Fourier and Fick’s laws over an inclined channel with applications of gold nanoparticles, *Sci Rep* 12 (2022) 17364.
- [199] F. Ali, A. Imtiaz, I. Khan, N. A. Sheikh, Flow of magnetic particles in blood with isothermal heating: a fractional model for two-phase flow, *J. Magn. Magn. Mater.* 456 (2015) 413-422.

- [200] N. Ali Shah, D. Vieru, C. Fetecau, Effects of the fractional order and magnetic field on the blood flow in cylindrical domains, *J. Magn. Magn. Mater.* 409 (2016) 10–19.
- [201] D. F. Jamil, S. Uddin, R. Roslan, The Effects of Magnetic Casson Blood Flow in an Inclined Multi-stenosed Artery by using Caputo-Fabrizio Fractional Derivatives, *J. Adv. Res. Mater. Sci.* 72(1) (2020) 15-30.
- [202] C. D. K. Bansi, C. B. Tabi, T. G. Motsumi, A. Mohamadou, Fractional blood flow in oscillatory arteries with thermal radiation and magnetic field effects. *J. Magn. Magn. Mater.* 456 (2018) 38–45.
- [203] D. Vieru, C. Fetecau, N. A. Shah, S-J. Yook, Unsteady natural convection flow due to fractional thermal transport and symmetric heat source/sink, *Alexandria Eng. J.* 64 (2023) 761 – 770.
- [204] S. He, N. A. A. Fataf, S. Banerjee, K. Sun, Complexity in the muscular blood vessel model with variable fractional derivative and external disturbances, *Physica A* 526 (2019) 120904.
- [205] P. K. Mandal, An unsteady analysis of non-Newtonian blood flow through tapered arteries with a stenosis, *Int. J. Non-Linear Mech.* 40 (2005) 151–164.
- [206] A.R. Pries, T.W. Secomb, P. Gaehtgens, Biophysical aspects of blood flow in the microvasculature, *Cardiovasc. Res.* 32 (1996) 654-667.
- [207] B. Chertok, A. E. David, V. C. Yang, Brain tumor targeting of magnetic nanoparticles for potential drug delivery: Effect of administration route and magnetic field topography, *J Control Release*, 155 (2011) 393-399.
- [208] P. D. Sorlie, M. R. Garcia-Palmieri, R Costas, R. J. Havlik, Hematocrit and risk of coronary heart disease: the Puerto Rico Heart Health Program, *American Heart Journal*, 101 (1981) 456-461.
- [209] World health organization, “cardiovascular diseases (CVDs)”, [https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)) (last accessed 25 January 2023).
- [210] N. Sher Akbar, S.U. Rahman, R. Ellahi, S. Nadeem, Nano fluid flow in tapering stenosed arteries with permeable walls, *Int. J. Therm. Sci.* 85 (2014) 54-61.
- [211] L. Xingting, C. Xingyu, Z. Yunwu, X. Jie, J. Xingcan, D. Tingting, Z. Yongfeng, D. Toghraie, M. Zarringhalam, The thermal behavior of blood flow in the arteries with

- various radii and various stenosis angles using non-Newtonian Sisko model, *Alex. Eng. J.* 61(2022) 7195-7201.
- [212] A. Zaman, N. Ali, N. Kousar, Nanoparticles (Cu, TiO₂, Al₂O₃) analysis on unsteady blood flow through an artery with a combination of stenosis and aneurysm, *Comput. Math. Appl.* 76 (2018) 2179-2191.
- [213] I. Cherkaoui, S. Bettaibi, A. Barkaoui, F. Kuznik, Magnetohydrodynamic blood flow study in stenotic coronary artery using lattice Boltzmann method, *Comput. Methods Programs Biomed.* 221(2022) 106850.
- [214] S.R. Yan, M. Zarringhalam, D. Toghraie, L.K. Foong, P. Talebizadehsardari, Numerical investigation of non-Newtonian blood flow within an artery with cone shape of stenosis in various stenosis angles, *Comput Methods Programs Biomed.* 192 (2020) 105434.
- [215] M. Timofeeva, A. Ooi, E.K.W. Poon, P. Barlis, Numerical simulation of the blood flow through the coronary artery stenosis: Effects of varying eccentricity, *Comput. Biol. Med.* 146 (2022) 105672.
- [216] A. Zaman, N. Ali, M. Sajid, Numerical simulation of pulsatile flow of blood in a porous-saturated overlapping stenosed artery, *Math. Comput. Simul.* 134 (2017) 1-6.
- [217] R. Bali, U. Awasthi, Effect of a magnetic field on the resistance to blood flow through stenotic artery, *Appl. Math. Comput.* 188 (2007) 1635–1641.
- [218] E. Amos, E. Omamoke, C. Nwaigwe, Chemical reaction, heat source and slip effects on MHD pulsatory blood flowing past an inclined stenosed artery influenced by body acceleration, *International Journal of Mathematics Trends and Technology* 68 (2022) 1-23.
- [219] M. K. Sharma, V. Nasha, P. R. Sharma, A study for analyzing the effect of overlapping stenosis and dilatation on non-Newtonian blood flow in an inclined artery, *J. Biomedical Science and Engineering*, 9 (2016) 576-596.
- [220] S.U. Siddiqui, C. Awasthi, Mathematical analysis on pulsatile flow through a catheterized stenosed artery, *J. Appl. Math. Phys.* 5 (2017) 1874–1886.
- [221] S. Das, T.K. Pal, R.N. Jana, B. Giri, Significance of Hall currents on hybrid nano-blood flow through an inclined artery having mild stenosis: Homotopy perturbation approach, *Microvasc. Res.* 137 (2021) 104192.

- [222] H. Badfar, Y.M. Saber, A. Sharifi, Numerical simulation of magnetic drug targeting to the stenosis vessel using Fe_3O_4 magnetic nanoparticles under the effect of magnetic field of wire, *Cardiovasc. Eng. Technol.* 11 (2020) 162-175.
- [223] R.X. Yin, D. Z. Yang, J.Z. Wu, Nanoparticle drug - and gene-eluting stents for the prevention and treatment of coronary restenosis, *Theranostics* 4 (2014) 175-200.
- [224] S. Sharma, U. Singh, V.K. Katiyar, Magnetic field effect on flow parameters of blood along with magnetic particles in a cylindrical tube, *J. Magn. Magn. Mater.* 377 (2015) 395–401.
- [225] S. Dhal, A. Mohanty, I. Yadav, K. Uvanesh, S. Kulanthaivel, I. Banerjee, K. Pal, S. Giri, Magnetic nanoparticle incorporated oleogel as iontophoretic drug delivery system, *Colloids Surf. B* 157 (2017) 118–129.
- [226] P.A. Voltairas, D.I. Fotiadis, L.K. Michalis, Hydrodynamics of magnetic drug targeting, *J. Biomech.* 35 (2002) 813-821.
- [227] M. Alishiri, S. Ebrahimi, P. Hemmati, A. Boroumand, A. Shamloo, Targeted drug delivery system using ultrasound transducers: A numerical study on stenosis artery, *28th National and 6th International Iranian Conference on Biomedical Engineering (ICBME)*, 107-111 (2021).
- [228] P. Nasimi, M. Haidari, Medical use of nanoparticles: drug delivery and diagnosis diseases, *Int. J. Green Nanotechnol.* 1 (2013) 1-5.
- [229] T. Hayat, M.I. Khan, M. Farooq, A. Alsaedi, M.I. Khan, Thermally stratified stretching flow with Cattaneo–Christov heat flux, *Int. J. Heat Mass Transf.* 106 (2017) 289–294.
- [230] M.A.A. Hamad, S.M.A. Gaied, W.A. Khan, Thermal jump effects on boundary layer flow of a Jeffrey fluid near the stagnation point on a stretching/shrinking sheet with variable thermal conductivity, *J. Fluids*, 2013 (2013) 74927.
- [231] T. Hayat, S. Qayyum, M. Imtiaz, A. Alsaedi, Impact of Cattaneo–Christov heat flux in Jeffrey fluid flow with homogeneous-heterogeneous reactions, *PLoS One*, 11 (2016) e0148662.
- [232] D. Tripathi, N. Ali, T. Hayat, M. K. Chaube, A. A. Hendi, Peristaltic flow of MHD Jeffrey fluid through finite length cylindrical tube, *Appl. Math. Mech.* 32 (2011) 1231–1244.
- [233] S.U. Rahman, R. Ellahi, S. Nadeem, Q.M. Zaigham Zia, Simultaneous effects of nanoparticles and slip on Jeffrey fluid through tapered artery with mild stenosis, *J. Mol. Liq.* 218 (2016) 484-493.

- [234] I. Ahmad and H. Ilyas, Homotopy perturbation method for the nonlinear MHD Jeffery–Hamel blood flows problem, *Appl. Numer. Math.* 141 (2019) 124-132.
- [235] M. Rafiq, M. Sajid, S.E. Alhazmi, M.I. Khan, E.R. El-Zahar, MHD electro osmotic peristaltic flow of Jeffrey nanofluid with slip conditions and chemical reaction, *Alex. Eng. J.* 61 (2022) 9977-9992.
- [236] S. Nadeem, N. Sher Akbar, and T. Naz, The numerical and analytical solution of peristaltic flow of a Jeffrey fluid in an inclined tube with partial slip, *J. Mech. Med. Biol.* 11 (2011) 773 – 802.
- [237] N. A. Mat Noor, S. Shafie, Y.S. Hamed, M.A. Admon, Soret and Dufour effects on MHD squeezing flow of Jeffrey fluid in horizontal channel with thermal radiation, *PLoS ONE* 17(2022) e0266494.
- [238] T. Hayat, R.Sajjad, S. Asghar, Series solution for MHD channel flow of a Jeffery fluid, *Commun. Nonlinear. Sci. Numer. Simul.* 15 (2010) 2400-2406.
- [239] S. Choudhary, P. Choudhary, B. Pattanaik, Tangent hyperbolic fluid flow under condition of divergent channel in the presence of porous medium with suction/blowing and heat source: Emergence of the boundary layer, *Int. J. Math. Math. Sci.* 2023 (2023) 6282130.
- [240] S. Choudhary, P. Choudhary, N. Alessa, K. Loganathan, MHD thermal and solutal stratified stagnation flow of tangent hyperbolic fluid induced by stretching cylinder with dual convection, *Mathematics*, 11(2023) 2182.
- [241] S. Choudhary, B. S. Yadav, “Reaction and thermal radiation on nonlinear mixed convective flow of Casson fluid over a vertical inclined porous plate embedded in porous medium,” *Int. J. Mod. Phys. C*, 32(20220) 9.
- [242] B. S. Yadav, S. Choudhary, Effect of melting heat transfer and thermal radiation on squeezing flow of a casson fluid with chemical reaction in porous medium, *Front. Heat Mass Transf.* 18 (2022) 18.
- [243] T. Anwar, P. Kumam, Asifa, I. Khan, P. Thounthong, Generalized unsteady MHD natural convective flow of Jeffery model with ramped wall velocity and Newtonian heating; A Caputo-Fabrizio approach, *Chin. J. Phys.* 68 (2020) 849-865.
- [244] M.A. Imran, F. Miraj, I. Khan, I. Tlili, MHD fractional Jeffrey’s fluid flow in the presence of thermo diffusion, thermal radiation effects with first order chemical reaction and uniform heat flux, *Results Phys.* 10 (2018) 10-17.

- [245] F. Ali, S. Murtaza, N.A. Sheikh, I. Khan, Heat transfer analysis of generalized Jeffery nanofluid in a rotating frame: Atangana–Baleanu and Caputo–Fabrizio fractional models, *Chaos Solitons Fractals* 129 (2019), 1-15.
- [246] X. Guo, J. Zhou, H. Xie, and Z. Jiang, MHD Peristaltic flow of fractional Jeffrey model through Porous medium, *Math. Probl. Eng.* 2018 (2018) 6014082.
- [247] X. Guo, H. Qi, Analytical solution of electro-osmotic peristalsis of fractional Jeffreys fluid in a micro-channel, *Micromechanics*, 8 (2017) 341.
- [248] I.A. Mirza, M. Abdulhameed, S. Shafie, Magnetohydrodynamic approach of non-Newtonian blood flow with magnetic particles in stenosed artery, *Appl. Math. Mech. - Engl. Ed.* 38 (2017)379–392.
- [249] S.U. Siddiqui, S.R. Shah, Geeta, A biomechanical approach to study the effect of body acceleration and slip velocity through stenotic artery, *Appl. Math. Comput.* 261(2015) 148–155.
- [250] A.M. Zidan, L.B. McCash, S. Akhtar, A. Saleem, A. Issakhov, S. Nadeem, Entropy generation for the blood flow in an artery with multiple stenosis having a catheter, *Alex. Eng. J.* 60 (2021)5741-5748.
- [251] S. Nallapu, G. Radhakrishnamacharya, Jeffrey fluid flow through porous medium in the presence of magnetic field in narrow tubes, *International Journal of Engineering Mathematics.* 2014 (2014) 713831.
- [252] R. Ponalagusamy, Particulate suspension Jeffrey fluid flow in a stenosed artery with a particle-free plasma layer near the wall, *Korea-Aust. Rheol. J.* 28 (2016)217-227.
- [253] R. Padma, R. Ponalagusamy, R.T. Selvi, Mathematical modeling of electro hydrodynamic non-Newtonian fluid flow through tapered arterial stenosis with periodic body acceleration and applied magnetic field, *Appl. Math. Comput.* 362 (2019)124453.
- [254] F. Ali, N.A. Sheikh, I. Khan, M. Saqib, Magnetic field effect on blood flow of Casson fluid in axisymmetric cylindrical tube: A fractional model, *J. Magn. Magn. Mater.* 423 (2017) 327–336.
- [255] S. Maiti, S. Shaw, G.C. Shit, Caputo–Fabrizio fractional order model on MHD blood flow with heat and mass transfer through a porous vessel in the presence of thermal radiation,” *Physica A* 540 (2020) 123149.

- [256] G.C. Shit, S. Majee, Pulsatile flow of blood and heat transfer with variable viscosity under magnetic and vibration environment, *J. Magn. Magn. Mater.* 388 (2015) 106–115.
- [257] G.C. Shit, S. Maiti, M. Roy, J.C. Misra, Pulsatile flow and heat transfer of blood in an overlapping atherosclerotic artery: a numerical study, *Math. Comput. Simul.* 166 (2019) 432–450.
- [258] N. A. Shah, D. Vieru, C. Fetecau, Effects of the fractional order and magnetic field on the blood flow in cylindrical domains, *J. Magn. Magn. Mater.* 409 (2016) 10–19.
- [259] S. Chien, R.G. King, R. Shalak, S. Usami, A.S. Copley, Viscoelastic properties of human blood and red cell suspensions, *Biorheology*, 12 (1975) 341-346.
- [260] R. E. Klabunde, *Cardiovascular Physiology Concepts* (third ed., Lippincott, Philadelphia, (2021).
- [261] S. Masashige, Y. Mitsugu, S. Masataka, H. Hiroyuki, W. Toshihiko, Y. Jun, K. Takeshi, Intracellular hyperthermia for cancer using magnetite cationic liposomes, *J. Magn. Magn. Mater.* 194 (1999) 176-184.
- [262] R. S. Molday, D. Mackenzie, Immuno specific ferromagnetic iron dextran reagents for the labeling and magnetic separation of cells, *J. Immunol. Methods.* 52 (1982) 353-367.
- [263] G. Mah, I. Zolotukhin, T. Fraites, J. Dobson, C. Batich, B. Byrne, Microsphere-mediated delivery of recombinant AAV vectors in vitro and in vivo, *Mol. Therapy.* (2000) 1-S239.
- [264] D. Panatarotto, C. D. Prtidos, J. Hoebeke, F. Brown, E. Kramer, J. P. Briand, S. Muller, M. Prato, A. Bianco, Immunization with peptide-functionalized carbon nanotubes enhances virus-specific neutralizing antibody responses, *Chemistry & Biology*, 10 (2003) 961-966.
- [265] P.F. Builders, M.I. Arhewoh, Pharmaceutical applications of native starch in conventional drug delivery, *Starch-Stärke.* 68 (2016) 864–873.
- [266] A. A. Alwan, S. Ahmed, A. Nwokoye, A. A. Alhendi, O. Ibrahim, E. Alhseinat, Recent advances in the application of magnetic/electromagnetic field for water desalination, Editor(s): A. Basile, E. P. Favvas, *Current Trends and Future Developments on (Bio-) Membranes*, (2024) 427-459.
- [267] Z. Tao, Z. Youcai, E. A. Nyankson, Integrated mechanical separation for municipal solid waste, Editor(s): Z. Tao, Z. Youcai, E. A. Nyankson, *Resource Recovery Technology for Municipal and Rural Solid Waste*, (2023) 77-83.