International Journal of Research in Pharmacy and Allied Science (IJRPAS)
Published by Ideal Publication
Available at https://idealpublication.in/ijrpas/

Computational Nano- Pharmacodynamics in Cardiovascular Diseases

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Article History
Received: 30/03/2023
Accepted: 02/05/2023
Published: 12/05/2023

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Abstract:
In industrialised nations, cardiovascular disease (CVD) is the vital cause of death and morbidity. Atherosclerotic lesions that narrow the arterial lumen are the cause of CVD. Development of plaque, reduces blood flow to the heart and usually causes serious consequences. Medication delivery methods alter the drug release profile, absorption, and distribution to treat various disorders while enhancing the effectiveness and safety of the final product. In the rapidly developing field of nanomedicine, materials on the nanoscale are employed as therapeutic agents. The nano-drug delivery system has distinguished itself as an excellent platform for delivering therapeutic agents to a sick location in a more regulated and targeted manner among all the other fascinating uses of nanomaterials. Through site-specificity, reduced toxicity, and target-oriented administration, nanotechnology aims to treat terrifying illnesses while providing various advantages. This review discusses new computer simulations of magnetically targeted nano-pharmacodynamics, nanoparticles, and nano-drug delivery devices.

Keywords: cardiovascular disease, nanomedicine, blood flow, arterial lumen, nano-pharmacodynamics, nano-drug delivery devices.

INTRODUCTION

Recent years have seen a significant increase in theoretical and experimental studies on the subject of blood flow in arteries with stenosis from a variety of angles in the field of vascular biomechanics, depending on the objectivity of the issues in the life sciences. The plasma that makes up about 55% of the total blood volume and is primarily made up of water, dissipated proteins, mineral ions, clotting factors, hormones, and blood cells is what makes up human blood, which is a heterogeneous multiphase suspension of blood cells (red blood, white blood, and platelets) . Although total blood has a non-Newtonian fluid character, it has been shown that plasma behaves like a Newtonian fluid . Blood has a Newtonian character for shear rates more

than 100 s-1, and this may be seen in big arteries, veins, and cavities, among other places. Blood behaviour, or hemo-rheological behaviour, is nonNewtonian for shear rates less than 100 s-1. One of the key parts of the circulatory system are the blood vessels. Veins are responsible for delivering deoxygenated blood towards the heart, while arteries transport oxygenated blood from the heart to various regions of the body. Capillaries, veins, and arteries make up the majority of the body's vessels. Capillaries typically measure 5 to 10 mm in diameter, but the diameter of veins ranges from 1 to 1.5 cm. Elastic arterial diameter is always more than 1 cm and for muscular arteries, it is about 0.1-10 mm. The thermophysical characteristics of blood are influenced by several factors, including temperature, age, and hematocrit. According to a theory put out by Whitmore in 1968, the blood arteries divide often, and their diameter changes with distance. According to Manton, the primary basis of a sizable class of issues with comprehending blood flows is the idea of flow in a changing cross-section. Although the precise cause of stenosis formation is unknown, its impact on flow characteristics has been studied both theoretically and empirically by numerous researchers. In order to understand how blood flow parameters, such as blood velocity, pressure, and shear stress, contribute to the development of stenosis and the efficacy of therapies, several studies have examined these factors

Table 1: Characteristics of Blood Cell

Blood Component	Per Microliter	Size (µm)	Percentage
Red blood cell	4.1-5.1 x 10^6	7-8	97
White blood cell			
Neutrophils (4-10 x 10^3)	62% of WBC	10-12	
Lymphocytes Eosinophils	30% of WBC	6-14	
Monocytes	2.3% of WBC	-	
Basophils	5.3% of WBC	15-20	
	0.4% of WBC	-	

Table 2: Characteristics of Plasma

Plasma Component	Component	Molecular Weight	Density (g/dl)
Plasma	Albumin	69000	4.5
Water 91%	Fibrinogen	340000	0.3
Protein 7%	Immunoglobulins	140000	2.5
	Prothrombin	68700	0.015
Other			
Salt includes vitamin,			
lipid, sugar etc.			

II. cardiovascular diseases

The development and progression of cardiovascular illnesses are fundamentally influenced by hemodynamic. Cardiovascular illnesses are brought on by the build-up of macrophage white blood cells, low-density lipoproteins (LDL), and cholesterol deposits on the arterial walls of blood vessels. This process causes the arteries to harden and reduce the cross-sectional area of the blood channel. Circulatory system disorders are common. These include several cardiovascular illnesses that impact the cardiovascular system, such as atherosclerosis, aneurysms, strokes, angina, etc., as well as lymphatic diseases that affect the lymphatic system. Many of these illnesses are referred to as "lifestyle diseases" because they progress gradually and are influenced by a person's eating patterns, exercise routines, smoking status, and other lifestyle decisions.

The capacity to correctly focus medications into a particular sick zone determines the best outcome for a wide range of cardiovascular disorders. Modern pharmacological formulations prevent the medication from accurately localising *end mass* at locations of interest despite extensive study and advancements in drug delivery. In many situations, the medication molecules disperse and spread at random throughout the body, leading to unfavourable side effects and a decrease in the active response to recommended dosages. Nano-fluid dynamics is a new subfield of fluid dynamics that focuses on fluids utilised in engineering at the nanoscale. Nanofluids have significantly improved a variety of applications in energy systems, business operations, transportation, the environment, and medicinal sciences.

III. Clinical significance

The World Health Organization (WHO) report 2019 states that CVDs are the leading cause of mortality worldwide, with more people dying each year than from any other cause combined. In 2016, 17.9 million deaths worldwide were attributed to CVDs or 31% of all fatalities. Heart attacks and strokes are to blame for 85% of these fatalities. The majority of CVD fatalities occur in low- and middle-income nations. In 2015, non-communicable illnesses caused 17 million premature deaths (before the age of 70), 82% of which occurred in low- and middle-income countries and 37% of which were attributable to CVDs. The majority of cardiovascular illnesses may be avoided by employing population-wide measures to target behavioural risk factors such as cigarette use, poor eating and obesity, inactivity, and problematic alcohol consumption. 28.1% of all fatalities in India in 2016 were caused by cardiovascular disorders. The leading risk factors for CVDs are high systolic blood pressure, air pollution, high cholesterol, dietary dangers, cigarette use, and a high body mass index.

IV. Nanofluids and application

Conventional fluids (air, water, oils, etc.) offer great lubricating properties in industrial applications, but their poor temperature characteristics severely limit their usage. These days, a lot of research is being done on ways

to speed up the heat transfer rates of common fluids. Experimental research has shown that adding tiny solid particles to the base fluid can significantly improve its thermo-physical characteristics.

The term "nanofluid," which Choi introduced in 1995, is a colloidal dispersion of particles between 1 and 100 nm in size in a base fluid. These nanoparticles can be liquid droplets, metallic, non-metallic, carbonic, oxide, carbide, metallic, non-metallic, and more. Water, mineral oil, ethylene glycol, or refrigerants all can be found in the base fluid. The Buongiorno model, a two-component nanoscale formulation emphasising Brownian motion and thermophoretic body force effects (originating in nuclear engineering at MIT), and the Tiwari-Das model, a volume-fraction based doping model, are the main foundations for both theoretical and experimental studies. Doping, or adding nanoparticles to base fluids, has been demonstrated to significantly boost thermal conductivity, which mainly accounts for the enhanced thermal performance of nanofluids. Because of how they interact with biological materials specifically, the nanoparticles used in biomedicine are also synthetic. Due to the nanofluid's better thermal conductivity over the traditional fluid, the rate of heat exchange in thermal systems is often increased by employing it. As a result, a thermal system's size may be optimised by transmitting a certain amount of heat, which makes the system smaller, by employing nanofluids to speed up heat transfer. In comparison to micro fluids, nanofluids are more stable and have a greater capacity to improve heat conduction. Nanofluids are replacing traditional fluids in many applications including heating and cooling.

V. Drug delivery system

A formulation or a device is referred to be a drug delivery system (DDS) if it makes it possible to introduce a therapeutic material into the body and increases its efficacy and safety by managing the rate, timing, and location of drug release. Drug delivery methods alter the drug's release profile, absorption, distribution, and elimination to increase product effectiveness and safety as well as patient convenience and adherence. Despite extensive research and development into medication delivery, the medicines are still unable to localise en mass to locations of interest due to current formulations. These medicine molecules scatter and disperse at random inside the body, causing unfavourable side effects that lessen the effectiveness of the right amounts. Nanofluid dynamics, a novel subfield of fluid dynamics that has applications in biology, medicine, and energetics, has emerged in recent years. In modern medicine, for instance, nano drugs are combined in microchannels for controlled distribution with bio-MEMS, which is a fundamentally different application of nanofluids (micro-electro-mechanical system). For this reason, medication delivery using nanoparticles holds enormous potential for therapies with few adverse effects and optimising precisely targeted distribution. Although the platform may increase a drug's tendency to accumulate at a specified site, it also encounters a complicated array of biological obstacles that restrict site-specific bioavailability, impeding the realisation of adequate therapeutic results.

The use of nanoparticles in therapy, diagnostics, coating medical devices, and medication administration is widespread. The magnetic targeted medication delivery system is one of the most alluring and effective methods for administering pharmaceuticals to the damaged spot. Due to their ability to reduce toxicity and other negative side effects, MTDDS are becoming more and more common in biomedicine. They are also fast-acting and extremely effective when compared to conventional approaches. Magnetic nanoparticle (MNP) uses in biomedicine might be either in vivo or in vitro, depending on the application. Applications for treatments and diagnostics are found in in-vivo settings, whereas applications for diagnostic use (separation/selection) are found in vitro settings. MNPs are frequently employed in gene therapy, targeted medication administration, electromagnetic hyperthermia, cell and macromolecule separation, and magnetic resonance imaging (MRI). MNPs, however stand out in particular because of their targeting capabilities. suitable for use with medication delivery systems.

The usage of iron oxides, and particularly magnetite, has been allowed by the Food and Drug Administration (FDA), which has also affirmed that these materials are completely safe for use by people. Health care has a lot of promise for nano-based medication delivery systems. Since their size enables for distribution through injection or other means, they offer higher drug penetration into the body. Nanoscience is being used in medicine to enhance the current approaches to treating certain conditions. A variety of active components targeted to lipid disorders, atherosclerosis-related angiogenesis, inflammation, and thrombosis prevention, among other ailments, may be delivered through controlled drug delivery systems using nanotechnology efficiently and securely. The development of iron oxide super-paramagnetic nanoparticles in magnetic drug targeting has been significant. The magnetic drug targeted system offers suitable magnetic gradients, increasing the concentration of nanoparticles at the affected region even more .

VI. Computational Nano-Pharmacodynamics/Nano-Hemodynamics

The field of research known as nano-pharmacodynamics or nano-hemodynamics has investigated several theoretical studies to demonstrate the impact of different nanoparticles (drugs) on blood flows. Due to its relevance in the fight against arteries with illness, stenotic nano-hemodynamics in particular has attracted a lot of attention in the engineering sciences and applied mathematics groups. Various computational techniques that are necessary to address the nonlinearity of the mathematical models were highlighted in the numerous research that has been documented. By utilising nanoparticles with a Prandtl blood flow mode and a homotopy perturbation approach, Nadeem et al. investigated the steady blood flow via tapered stenosed arteries. Ahmed et al. studied the effects of several nanoparticles (Cu, TiO2, and Al2O3) on Newtonian blood flow in a single stenosed channel and found that Al2O3 nanoparticles had a higher flow acceleration in the core area than either Cu or TiO2 nanoparticles. Using Buongiorno's model and the forward time central space (FTCS) approach, Ali et al. performed a numerical simulation of the time-dependent non-Newtonian (Sisko fluid) nano pharmacodynamic transport phenomena in an overlapping tapering artery. The finite element technique (FEM) was used to confirm the results, and it was discovered that the flow rate at the stenotic neck

reduces as the Brownian motion parameter rises. A robust model of non-Newtonian nanofluid hemodynamics with heat and mass diffusion in a stenosed coronary artery in the presence of a radial magnetic field has just been created by Vasu et al. To help you comprehend the role of nano-drug diffusion in the therapy of cardiovascular illness, we'll briefly go over some of the simulation's specifics here (stenotic arteries). The formulation makes use of both Buongiorno's nanoscale model and the Reiner-Rivlin second-order differential model.

The hemodynamic properties in this study were computed using the FreeFEM++ finite element algorithm. As shown in Figure 6, the finite element mesh was created using 5928 unstructured fixed triangular elements with 12177 nodes. The automated FreeFEM++ mesh generator, which is based on the Delaunay-Voronoi technique, was used to create the mesh.

Therefore, the maximum magnetic and thermophoresis parameter values work together to significantly reduce nanoparticle concentration values. Therefore, using a weaker magnetic field and lower thermophoresis in nano-particle deployment in stenotic blood flows may result in the opposite effect, elevation in nanoparticle diffusion. Modern nano-biomedicine and drug delivery systems obviously benefit from the visualisation capability of computational nanohemodynamics, which also offers an ideal approach for maximising the effects of various nano-drugs in clinical therapies. Other numerical approaches, such as Lattice Boltzman, molecular dynamics, smoothed particle hydrodynamics, and boundary element techniques, are also extremely promising in this area.

Conclusion

Along with improvements in the distribution of prescription pharmaceuticals via novel treatment techniques, current developments in nanomedicine have also been taken into account in this study. The primary reason for using nanotechnology in biomedicine is to improve the solubility, bioavailability, absorption, and targeted and controlled release of medications. The effectiveness of conventional pharmacological agents is significantly increased by the use of nano-carriers formulated with dendrimers, liposomes, micelles, solid lipid nanoparticles, gold, silver, titanium oxide, and cadmium sulphide polymeric nanoparticles along with superparamagnetic iron oxide nanoparticles. Due to their special qualities, magnetic drug delivery systems have great potential for targeted and controlled distribution. In addition, this study has discussed important developments in the application of computational and mathematical hemodynamic models to simulate the effects of nanoparticle medication delivery in cardiovascular disorders (stenotic arteries, aneurysms, etc.). A deeper understanding of the underlying processes involved in nano-drug delivery is made possible by computational nano-pharmaco/hemodynamics, which has several benefits. In this regard, several techniques have been created, and they all call for more research and clinical evidence to support them. Using computer modelling approaches will significantly speed up the development of nano-biomedicine, as well as increase safety and minimise toxicity.

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