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Research Article

Assessing the Influence of Glucosamine Supplementation on Synovial Fluid Dynamics in Osteoarthritic Knee Joints

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Abstract

Osteoarthritis (OA) is a prevalent joint disorder characterized by the degeneration of articular cartilage, leading to pain, stiffness, and impaired joint function. Synovial fluid plays a crucial role in maintaining joint health by providing lubrication, shock absorption, and nutrient supply to the articular cartilage. In Osteoarthritis, alterations in synovial fluid composition and flow dynamics contribute to disease progression and symptom severity. Glucosamine, a popular dietary supplement, is widely used for its purported benefits in managing Osteoarthritis symptoms and potentially slowing disease progression. Understanding how glucosamine affects synovial fluid dynamics in osteoarthritic knee joints is essential for optimizing treatment strategies and improving patient outcomes. Our research focuses on investigating the impact of glucosamine supplementation on synovial fluid dynamics within the knee joint of individuals with Osteoarthritis. Using computational modeling and simulation techniques, we explore the complex interplay between synovial fluid flow, cartilage health, and glucosamine supplementation. By analyzing synovial fluid flux in both the joint cavity and articular cartilage, we aim to elucidate how glucosamine influences fluid dynamics and joint biomechanics in osteoarthritic knees. Through our computational simulations, we assess the pressure gradient-induced flow of synovial fluid and its variations in response to glucosamine supplementation. Graphical representations of our findings provide insights into the underlying mechanisms driving synovial fluid dynamics and highlight the influence of glucosamine on these processes. By examining the effects of glucosamine on key model parameters, such as synovial fluid viscosity, cartilage integrity, and inflammatory markers, we aim to delineate the mechanisms through which glucosamine may exert its therapeutic effects in Osteoarthritis.

Keywords: Firfire; Osteoarthritis; Fluid Flux; Hyaluronic Acid; Synovial Cavity; Articular Cartilage; Glucosamine Supplementation; Joint Health; Disease Progression; Therapeutic Interventions.

Introduction

Synovial joints play an indispensable role in facilitating human movement, serving as pivotal points for essential activities such as walking, running, and bending. These joints can be visualized as sophisticated load-bearing systems composed of two connected bones that articulate and move in various directions. At the ends of these bones, typically spherical in shape, lies a soft, sponge-like material known as articular cartilage (Akinsola and Temitayo, 2019; Kasturia, 2024: Kumar and Shah, 2024; Shah, 2022). This specialized cartilage provides a smooth surface for bone movement and serves as a protective cushion, preventing friction and wear. Within the joint cavity, the space between the cartilaginous ends of the bones, resides synovial fluid a remarkable fluid with unique properties crucial for joint

function (Chaturvedi *et al*., 2021; Shah, 2011; Siddiqui and Shah, 2016; Tasneem *et al*., 2024). Synovial fluid, transparent and thin in consistency, closely resembles plasma in its composition. It contains essential components such as hyaluronic acid and lubricin, along with glycoproteins and proteinase enzymes. These constituents work harmoniously to provide lubrication, nourishment, and protection to the joint structures. Synovial fluid acts as a lubricating agent, facilitating smooth movement and reducing friction between the articular surfaces during joint motion (Shah and Kumar, 2018; Chaturvedi and Shah, 2023; Gupta *et al*., 2024, Shah, 2011). This intricate interplay between articular cartilage and synovial fluid forms the foundation of synovial joint function, influencing their behavior and overall health. Lubricin, a crucial protein found in synovial fluid, plays a pivotal role in ensuring the smooth operation of joints (Islam *et al*., 2023; Shah, 2010; Kumar and Shah, 2022; Jaiswal *et al*., 2024; Shah, 2012). This protein is primarily responsible for providing lubrication to the joint surfaces, reducing friction, and preventing wear and tear. Additionally, synovial fluid serves as a vital source of nutrition for the cells residing in the articular cartilage, supporting their metabolic activities and maintaining tissue health. Among synovial joints, the human knee joint stands out as one of the most significant, enabling various essential activities such as walking, running, and jumping (Kumar and Shah, 2021; Sadique and Shah, 2023; Malik, 2020; Shah, 2011).

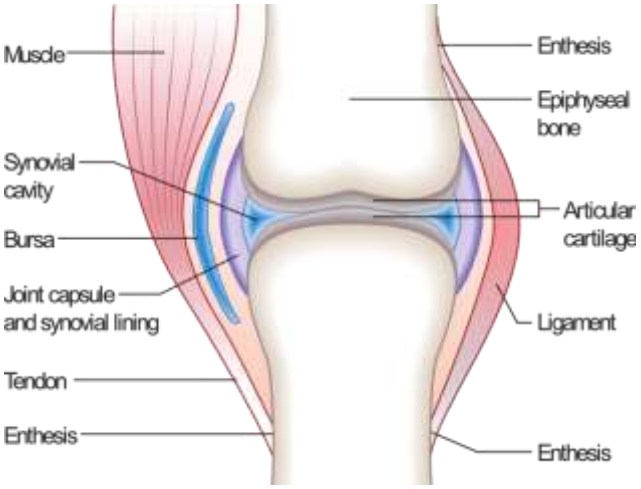

Fig.1: Structure and function of synovial joints

Comprising three main components synovial fluid, articular cartilage, and synovial membrane the knee joint is a complex structure designed to withstand considerable forces. Geometrically, the knee joint can be conceptualized as divided by cylindrical surfaces, allowing for efficient movement and load distribution. Remarkably, the knee joint is engineered to bear loads up to four times the body weight, highlighting its robust nature (Akbar, 2024; Shah, 2014; Stiehl *et al*., 2024; Shah and Siddiqui, 2012). Articular cartilage, a critical component of synovial joints, is a pale connective tissue composed of specialized cells known as chondrocytes. Hydrated and porous, cartilage serves as a cushioning material, absorbing shock and distributing pressure evenly across the joint surfaces (Akbar and Shah, 2024; Akinsola and Temitayo, 2014; Geeta *et al*., 2014; Kumar and Shah, 2017). In addition to traditional lubrication methods involving fluid film or boundary lubrication, cartilage exhibits unique lubrication mechanisms that contribute to joint function and longevity. The current study delves into the intricate dynamics of synovial fluid flow within the context of synovial joints, particularly focusing on the knee joint (Shah, 2021; Singh *et al*., 2016; Shah, 2017; Majhi *et al*., 2024; Singh, 2010). By employing mathematical models such as the Navier-Stokes and Brinkman equations, researchers aim to elucidate the influence of synovial fluid viscosity, articular cartilage permeability, and other joint properties on fluid flow patterns (Shah, 2013; Siddiqui, 2016; Shah, 2014; Singh, 2010). This investigation holds promise for enhancing our understanding of synovial joint physiology, shedding light on pathological conditions and offering insights into potential therapeutic strategies. Moreover, it underscores the significance of long-chain hyaluronic acid molecules in synovial fluid, emphasizing their role in joint lubrication and health.

Formulation of Mathematical Model

In our study, we've employed the Navier-Stokes Equations and Brinkman equation to model the flow of synovial fluid within the joint cavity and articular cartilages, respectively. To simplify the analysis, we've made several assumptions about the synovial fluid, considering it to be Newtonian, incompressible, non-conducting, and non-magnetic (Shah, 2011; Singh, 2011; Anamika, 2017, Siddiqui, 2015, Singh *et al*., 2016). Additionally, we've assumed the flow to be steady and laminar, meaning there's no fluctuation of any synovial fluid parameter with time. Moreover, we've disregarded pressure fluctuations throughout the fluid layer thickness and negligible external forces. Although some external forces exist, their impact is minimal. We have also applied the no-slip boundary conditions at the surfaces of the cartilage. With these assumptions in place, the Brinkman equation and the Navier-Stokes equation are simplified to regulate the flow of synovial fluid within the diseased human knee joint Fig.1.

$$\mu \frac{\partial^2 u}{\partial y^2} - \frac{\partial p}{\partial x} = 0 \qquad (1)$$

$$\mu' \frac{\partial^2 v}{\partial y^2} - \frac{\mu}{\varphi} v - \frac{\partial p}{\partial x} = 0 \qquad (2)$$

Equation (1) represents a simplified version of the Navier-Stokes equation, which we derived by applying our set of assumptions. On the other hand, Equation (2) is the Brinkman equation, an extension of Darcy's law specifically designed to describe fluid flow through porous media (Stiehl *et al*., 2024; Shah and Kumar, 2020; Singh and Shah, 2010; Chaturvedi and Shah, 2024). The symbols μ, μ', and

φ represent different properties related to the synovial fluid and articular cartilage. Specifically, μ stands for viscosity, μ' represents the apparent viscosity of the synovial fluid, and φ denotes the permeability of the articular cartilage (Shah, 2011; Singh, 2011; Shah, 2013; Sadiqui, 2022, Geeta *et al*., 2015). The conditions that apply to the synovial fluid as it moves through the thin layer of fluid in the synovial cavity and across the articular cartilage are described as follows:

$$\frac{\partial u}{\partial y} = 0 \qquad at \qquad y = 0 \quad (3)$$

$$v = 0 \qquad at \qquad y = h + H \quad (4)$$

In simpler terms, the boundary condition described in equation (4) is based on the principle of no-slip, meaning the synovial fluid doesn't slip past the stationary articular cartilage. At the interface where the synovial fluid meets the cartilage, the fluid's velocity matches that of the cartilage because of this no-slip rule. This matching of velocities ensures that there's no sliding between the fluid and the cartilage surface (Kumar, 2017; Lenin, 2024; Geeta *et al*., 2015; Siddiqui, 2016) The shear stress experienced by the synovial fluid due to its properties being Newtonian and flowing in layers is directly related to the rate at which it deforms, with viscosity acting as the factor of proportionality. Since the shear stress must be the same at the boundary, we establish a condition where the shear stresses match.

$$\mu \frac{\partial^2 u}{\partial y^2} = \mu' \frac{\partial^2 v}{\partial y^2} \qquad at \qquad y = h \quad (5)$$

With our assumption that there is no slipping at the boundary, the velocity of the synovial fluid within the fluid film and the articular cartilage at their interface must be identical. This means that where the synovial fluid film and the articular cartilage come into contact, their velocities match. Therefore, the conditions for matching velocities at the interface are as follows:

$$u = v = V \qquad at \qquad y = h \quad (6)$$

This equation describes the velocity of the synovial fluid at the interface where the articular cartilage and fluid film meet, denoted by V.

After applying the boundary condition from equation (3) and the matching condition from equation (6) to equation (1), we derived the expression for the velocity of the synovial fluid in the fluid film, represented as follows:

$$u = \frac{1}{\mu}\frac{\partial p}{\partial x}(y^2 - h^2) + V \quad (7)$$

By utilizing the boundary condition described in equation (4) and the matching condition outlined in (6), we solve equation (2) to determine the velocity of the synovial fluid within the articular cartilage. The resulting expression for this velocity is as follows:

$$v = \left[\left(\frac{\varphi}{\mu}\frac{\partial p}{\partial x}\frac{1}{\sinh(MH)}\right) sinhM(h + H - y) - sinhM(h - y) - sinhMH)\right] + \left[\frac{VsinhM(h + H - y)}{sinhMH)}\right] \quad (8)$$

Applying the stress matching condition specified in equation (5), we derive the velocity of the synovial fluid at the interface. Consequently, the expression for this velocity at the interface is as follows:

$$V = \frac{\varphi}{\mu}\frac{\partial P}{\partial x}\tanh(MH)\left(tanh\frac{MH}{2} - Mh\right) \quad (9)$$

Hence, the ultimate expressions for the velocities of the synovial fluid in the fluid film and articular cartilage are given below:

$$u = \frac{1}{\mu}\frac{\partial p}{\partial x}(y^2 - h^2) + \left[\frac{\varphi}{\mu}\frac{\partial P}{\partial x}\tanh(MH)\left(tanh\frac{MH}{2} - Mh\right)\right] \quad (10)$$

$$v = \left[\left(\frac{\varphi}{\mu}\frac{\partial p}{\partial x}\frac{1}{\sinh(MH)}\right) sinhM(h + H - y) - sinhM(h - y) - sinhMH)\right] + \left[\frac{VsinhM(h + H - y)}{sinhMH)}\right] \quad (11)$$

So, at any moment, the synovial fluid flux through a cartilage and fluid film represents the quantity of fluid flowing through them per unit time. This is calculated by summing up the velocity across the cartilage and fluid film. Consequently, the synovial fluid flux is determined by integrating the velocity over the range of y from zero to a final value (h+H). The synovial fluid flux Q is calculated using the following equation:

$$Q = \int_0^h u\,dy + \int_h^{h+H} v\,dy \qquad (12)$$

So, by integrating the values of u and v obtained from equations (10) and (11) over the respective film and cartilage thickness, we arrive at the ultimate expression for the synovial fluid flow in both the articular cartilage and synovial fluid film within the joint cavity. The expression for the synovial fluid flux is given by:

$$Q = -\frac{\partial P}{\partial x}\left[\frac{1}{M^3\mu'}\left(tanhMH\left(Mh - tanh\frac{MH}{2}\right)^2 + MH + 2tanh\frac{MH}{2}\right) + \frac{h^3}{3\mu}\right] \qquad (13)$$

Results and Discussion

We have conducted computational simulations using our proposed model to analyze the flow of synovial fluid within the joint cavity and articular cartilage. To achieve this, we applied relevant physiological parameters and employed the Navier-Stokes and Brinkman equations. The results, along with the impact of key parameters on the flow, have been depicted through graphs. These graphs, spanning from Fig. 2 to 6, showcase how flux varies with parameters like permeability, film thickness, and cartilage thickness. MATLAB was utilized to gather numerical data for viscosity, flow rate, cartilage permeability, film thickness, and synovial fluid flux. All parameter values were sourced from existing literature to ensure diverse synovial fluid flow patterns were generated. The impact of glucosamine supplementation on viscosity, specifically in the context of osteoarthritic knee joints, has been a subject of interest in various studies. Glucosamine is a naturally occurring compound that is believed to play a role in cartilage health and repair. We have investigated the effects of glucosamine supplementation on synovial fluid viscosity, which is crucial for joint lubrication and function. While the results have been somewhat mixed, some studies suggest that glucosamine may have a positive impact on synovial fluid viscosity. One possible mechanism by which glucosamine may affect viscosity is by promoting the production of hyaluronic acid, a key component of synovial fluid that helps lubricate and cushion the joints. Glucosamine has been shown to stimulate the synthesis of hyaluronic acid in joint tissues, which could potentially lead to an increase in synovial fluid viscosity. The impact of glucosamine supplementation on the flow flux of synovial fluid, especially in the context of osteoarthritic knee joints, is an area of interest for researchers studying joint health and function. Glucosamine, a natural compound found in the body, is often used as a dietary supplement to support joint health and alleviate symptoms of osteoarthritis. It is believed to play a role in cartilage repair and maintenance. Synovial fluid dynamics, including its flow flux, are crucial for joint lubrication, nutrient distribution, and waste removal within the joint space. The exact impact of glucosamine on synovial fluid flow flux remains unclear and may depend on various factors, including the severity of osteoarthritis, the dosage and duration of glucosamine supplementation, and individual patient characteristics. We obtained that glucosamine supplementation may promote the production of hyaluronic acid, a key component of synovial fluid, which could potentially enhance synovial fluid flow flux by improving its lubricating properties and viscosity.

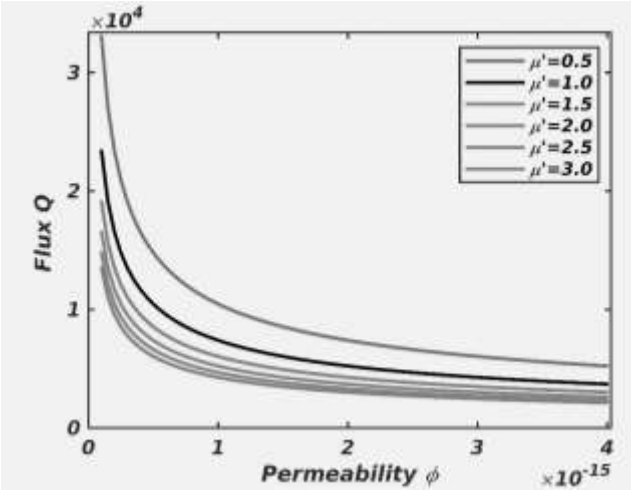

Fig. 2: Variation of Flux with Permeability for Apparent Viscosity.

In Fig. 3, we observe the variation in flux concerning permeability across different values of apparent viscosity. The trend depicted illustrates a decrease in flux as permeability increases. This downward trend in synovial fluid flux with increasing permeability is consistent across various parameters. Upon closer examination of subfigures within the same parameter, we note an increase in fluid flux concerning viscosity, pressure gradient, and film thickness, whereas a decrease is observed concerning apparent viscosity (Anamika *et al*., 2017; Shah, 2013; Kumar, 2017). Synovial fluid flux is directly influenced by the viscosity of the synovial fluid, the thickness of the fluid film, and the pressure gradient within the film. Conversely, it is inversely affected by the apparent viscosity of the synovial fluid. Hence, it can be concluded that synovial fluid flux rises with an increase in the pressure gradient within the fluid film, the viscosity of the synovial fluid, and the thickness of the fluid

film. Conversely, it declines with an increase in the apparent viscosity of the synovial fluid.

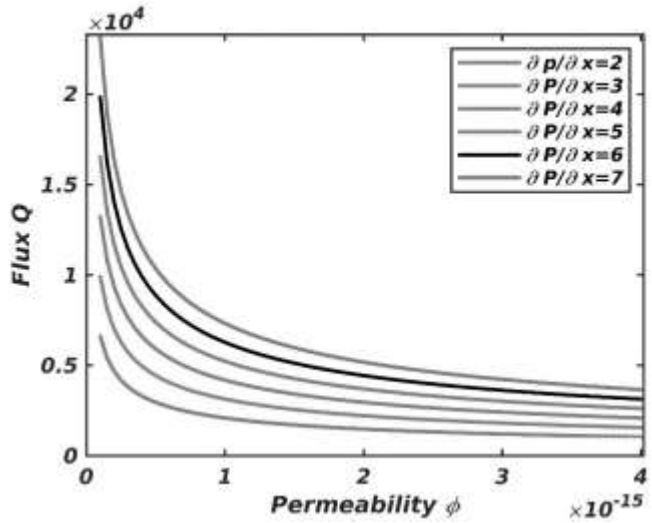

Fig. 3: Variation of Flux with Permeability for Pressure Gradient

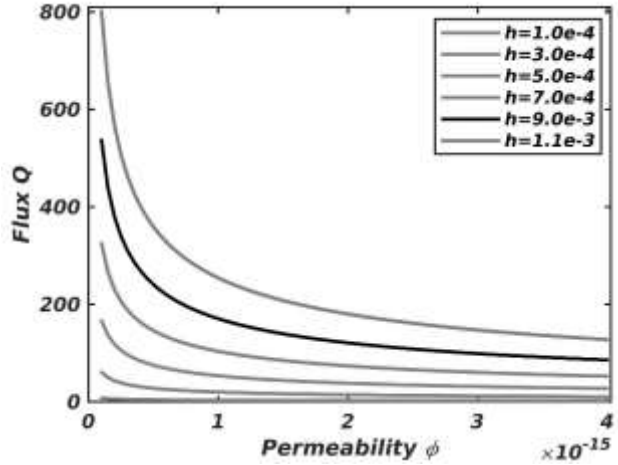

Fig. 4: Variation of Flux with Permeability for Film Thickness

In Fig. 4, we observe how flux varies with permeability across different pressure gradient values. Generally, flux increases with the thickness of the fluid film across all parameters. The depicted trend illustrates a decrease in flux with increasing permeability and pressure gradient, while it decreases with viscosity and apparent viscosity as well. Synovial fluid flux is directly linked to articular cartilage permeability and fluid film thickness, while it is inversely related to the viscosity and apparent viscosity of the synovial fluid (Kumar, 2017; Geeta *et al*., 2016). Based on these observations, we can infer that synovial fluid flux rises with an increase in the pressure gradient within the fluid film and the permeability of the articular cartilage. Conversely, it declines with an increase in the viscosity and apparent viscosity of the synovial fluid. Fig. 5 illustrates how flux changes concerning the thickness of articular cartilage across various viscosity values of synovial fluid. We observe that flux remains constant with cartilage thickness for all parameters except synovial fluid viscosity. The sole factor influencing flux along the articular cartilage thickness is the viscosity of the synovial fluid (Shah, 2011, Kumar *et al*., 2024). There exists a linear relationship between flux and articular cartilage thickness, with higher flux observed when the viscosity of the synovial fluid is lower. Conversely, when the viscosity of the synovial fluid is higher, the synovial flux decreases in articular cartilages. Therefore, it can be deduced that synovial fluid flux in articular cartilage increases as the viscosity of the synovial fluid rises.

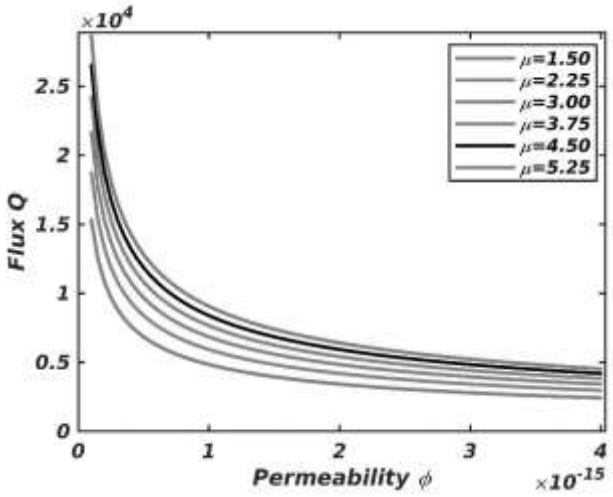

Fig. 5: Variation of Flux with Permeability for Viscosity

Conclusion

The primary aim of this study was to develop a straightforward mathematical model to elucidate how synovial fluid flows in diseased human knee joints. We've generated computational results to depict synovial fluid flow caused by pressure gradients within the knee joint. These results have been visually presented through graphs to unravel the flow mechanism and analyze the impact of various model parameters on fluid flow. Our investigation primarily focused on examining synovial fluid flux within the synovial cavity and articular cartilage. By studying pressure-gradient induced synovial fluid flow, we gained insights into the behavior of synovial fluid within the knee joint. The data obtained from our computational analysis have been graphically represented to facilitate a better understanding of fluid flow dynamics and the influence of model parameters. We observed that synovial fluid flux increases as the thickness of the synovial fluid film between articular cartilages increases, while it decreases with higher permeability of the articular cartilage. This indicates that decreased viscosity of synovial fluid in diseased conditions leads to freer flow during the squeezing process, resulting in a reduced amount of synovial fluid remaining in the joint cavity. Consequently, the knee joint becomes less lubricated and more prone to damaging the articular cartilage through

friction. Additionally, we noted a decrease in articular cartilage permeability in diseased conditions, which led to a reduction in synovial fluid flow. These findings provide valuable insights into identifying factors contributing to medical issues in the knee joint. Furthermore, they enhance our understanding of how synovial fluid flow influences the development of joint diseases. Ultimately, this study may contribute to the development of therapeutic approaches aimed at addressing pathological conditions in the human knee joint.

Authors' Contribution

All authors contributed equally at all stages of research, data analysis and manuscript preparation. Final form of manuscript was approved by all authors.

Conflicts of Interest

The authors declare that there is no conflict of interest related to this work.

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