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Role of hydrophobicity on the adsorption of synovial fluid proteins and biolubrication of polycarbonate urethanes: Materials for permanent meniscus implants

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ABSTRACT

Both absorption and release of synovial fluid components lubricate the porous natural meniscus, whereas only adsorption can lubricate non-porous meniscus prostheses. The aim of this study was to establish the adsorption characteristics of the synovial fluid proteoglycan 4 (PRG4) and albumin on modified and unmodified polycarbonate urethane (PCU) and determine the effects on the coefficient of friction. PCU was modified with surface-tethered C18 chains (mPCU). Self-assembled monolayers (SAM) on gold were also used to generate higher and lower hydrophobicities. Protein adsorption and coefficients of friction were measured by quartz crystal microbalance and colloidal probe atomic force microscope. PRG4 formed a thick viscoelastic layer and significantly decreased the coefficient of friction on PCU and mPCU, with an exceptionally low coefficient of friction measured on mPCU (0.02 ± 0.02) due to its soft surface. Albumin formed a thin rigid layer with a much higher coefficient of friction on mPCU (1.14 ± 0.19). Albumin blocked PRG4 adsorption when simultaneously added to PCUs, and coefficients of friction of 0.48 ± 0.24 (PCU) and 0.49 ± 0.17 (mPCU) were measured. Albumin adsorption on hydrophobic substrates (water contact angle $\geqslant 70° \pm 4°$) dramatically increased the coefficient of friction (3.41 ± 1.21 on hydrophobic SAM), indicating that increased hydrophobicity through hydrocarbon surface modification of PCU carries tribological risks.

1. Introduction

Meniscal injury in the form of a tear is one of the most common sports related injuries in young patients. Meniscal tears often occur due to the posterior displacement of the medial meniscus as a response to the external rotation of the tibia on the flexed femur [1]. Left untreated, the injury may lead to cartilage damage and signs of early arthritis. Considering the fact that menisci have a very limited ability to regenerate and heal, once damaged, they cause serious problems [1]. The menisci in the knee joint play important roles in load bearing, load distribution, shock absorption, proprioception and lubrication of the joint. Furthermore this tissue also acts to provide nutrition to the articular cartilage and behaves as secondary stabilisers [2]. The loss of menisci function leads to degeneration of the joint due to changes in the cartilage load distribution [3]. In the synovial joints the terminal portion of bone is covered with a thin layer (1–5 mm) [4] of hydrated, avascular hyaline tissue called articular cartilage which plays an important role in lubrication during articulation and load distribution in the joint [5]. Articular cartilage consists of 70–80% water, and its dry weight contains 2% chondrocytes and 98% extra-cellular matrix (ECM) produced by the chondrocytes. ECM is composed of 50–75% collagen (90% collagen type II), 15–30% proteoglycans (mainly aggrecan) and 10% lipids (mainly phospholipids) [5,6]. Meanwhile menisci are crescent-shaped, biphasic composite materials which play many important roles in the knee joint. The fibro-cartilaginous tissue of the meniscus consists of water as a major component (63–75% of the total weight). The dry weight consists of 75% collagen (mostly collagen type I) and 2.5% proteoglycan [7].

As a treatment for meniscal injury, total or partial meniscectomy is commonly performed. Clinical studies show that both types of meniscectomy increase the risk of osteoarthritis in the knee due to the decreased stress distribution [3,8]. Therefore, surgeons prefer to repair the injured meniscus. However, when this is not possible, the meniscus is replaced with an allograft to protect the articular cartilage from damage [9]. An allograft meniscus

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transplant alleviates pain and improves function as well as having a satisfactory survival rate [10,11]. Drawbacks of these allografts are limited availability, size mismatching, high costs, graft shrinkage after implantation and risk of transmission of disease [12,13]. Alternatively, there are several biodegradable implants based on synthetic and natural polymers available but these implants demonstrate other disadvantages such as lack of durability in loading conditions [14–16].

The development of permanent meniscus prostheses is a promising alternative to the above treatments. Such a prosthesis needs to remain in place and perform for many years. The challenge is thus to find a biomaterial that is able to withstand the loading forces in the joint, is chondroprotective and yields effective tribological properties in the presence of synovial fluid.

Healthy diarthrodial or synovial joints provide ultralow coefficients of friction (0.001–0.005) and excellent wear protection between the articulating surfaces during lifetime in the body [17]. These sophisticated tribological properties are due to unique lubrication mechanisms inside the joints which are difficult to achieve in artificial systems [18]. Several descriptions of these mechanisms have been proposed: hydrodynamic lubrication [19,20], boundary lubrication [21,22], elasto-hydrodynamic lubrication [23,24], weeping lubrication [25], boosted lubrication [26], squeeze-film lubrication [27,28] and biphasic lubrication [29]. The lubrication mechanisms are not mutually exclusive, and the predominant form will depend upon the loads and speed. There is now a general agreement that under high load and low sliding speeds boundary lubrication is the most important mechanism in play [30,31].

In the knee joint the porous nature of the cartilage and meniscus tissue and the presence of viscous synovial fluid play critical roles in the lubrication process. Water is the major component of synovial fluid along with different inorganic (Table 1) and organic (Table 2) components. A high concentration of hyaluronan (HA) is responsible for the high viscosity of the fluid [32,33]. A glycoprotein proteoglycan 4 (PRG4, also known as lubricin) mainly secreted by superficial layer chondrocytes [34,35] and surface active phospholipids (SAPL) are known to be involved in the joint lubrication [17,36]. Albumin, a globular protein, is the most abundant protein present in synovial fluid [37]. Despite this fact albumin does not play a key role as a boundary lubricant on the natural cartilage or meniscus surface [38,39], but it is known to decrease the wear rate of ultrahigh molecular weight polyethylene (UHMWPE) acetabular cups against metallic heads used in the artificial joints [40]. However, joint diseases, such as osteoarthritis and rheumatoid arthritis, or injuries could change the chemical environment in the joint which influences cells and the secretion of the lubricant molecules (HA, PRG4 and SAPL) by them [41]. Joint diseases and injuries also change synovial membrane permeability, and consequently the filtration of plasma proteins (albumin) [42]. Therefore, the composition of rheumatoid or osteoarthritic synovial fluid changes [41,42]. Clinical studies have shown that in humans, HA concentration could decrease down to 0.1 g/L due to arthritis, while albumin, PRG4 and SAPL concentrations could increase up to 20 g/L, 0.762 g/L and 0.8 g/L respectively [39,42].

As per the fluid pressurization and weeping model the porous, natural meniscus absorbs synovial fluid and releases it upon loading keeping the opposing sliding surfaces spaced apart [32,36,39]. Meanwhile, the proteinaceous components of the synovial fluid adsorb onto both meniscus and cartilage surfaces providing boundary lubrication under high loads and low sliding velocities [32,36,39]. For an artificial nonporous meniscus, the only way to achieve effective lubrication at points of high contact pressures is through the adsorbed layer of lubricating molecules, e.g., PRG4, HA and SAPL.

Table 1
Concentrations of the major inorganic components of normal synovial fluid.

Component	Concentration (mmol/L)
Sodium	133–139 [69]
Potassium	3.5–4.5 [69]
Chloride	87–138 [69]

Table 2
Concentrations and molecular weights of some of the major organic components of normal synovial fluid.

Component	Molecular weight (kDa)	Concentration (g/L)
Hyaluronan	500–6000 [32,33]	1–4 [32,33]
Proteoglycan 4	230–460 [34,35]	0.052–0.350 [34,35]
Surface active phospholipid	0.73 [70,71]	0.100–0.200 [70,71]
Albumin	70 [37]	4–10 [37]

Polycarbonate urethane (PCU) is currently used for making a synthetic meniscus implant (NUsurface® by Active Implants, Israel) to replace the damaged meniscus [43,44]. The PCU meniscus is very well studied for its biomechanical characteristics [43], but the tribological characteristics in the synovial joint milieu still require attention.

The first aim of this study was to investigate the adsorption of synovial fluid proteins, i.e., PRG4 and albumin, on PCU as well as the resulting biolubrication. HA was not included in the study, because preliminary experiments demonstrated that HA did not adsorb to any of the surfaces. Albumin has been shown to decrease wear of UHMWPE and it is important to be considered due to its abundance in synovial fluid. Especially since in salivary lubrication albumin is known to interfere with the adsorption of mucin to surfaces [45].

The second aim of this study was to investigate the role of hydrophobicity of the material on the protein adsorption and resulting biolubrication. PRG4 molecules are known to adsorb very well on hydrophobic surfaces [46,47], and are thus expected to do the same on PCU, which is moderately hydrophobic. To enhance this effect, a modified PCU (mPCU), containing surface-tethered C18 chains, has been studied as well. To further increase the range of hydrophobicity, self-assembled monolayers (SAM) terminating in hydroxyl or methyl groups were made over gold sensors to create a very hydrophilic and a very hydrophobic substratum respectively.

Quartz crystal microbalance with dissipation (QCM-D) was used to investigate the adsorption mechanisms and kinetics of PRG4 and albumin, applied individually or simultaneously, on surfaces of PCU, mPCU, the hydrophobic SAM and the hydrophilic SAM on gold. QCM-D is a non-destructive and non-invasive, acoustic sensing technique. It provides real-time information of the adsorption process *in situ*, such as the adsorption kinetics of the molecules (PRG4 and albumin in this study), the quantity of the adsorption and the structure of the adsorbed layer at solid–liquid interfaces [48]. Afterwards the samples with adsorbed molecules were subjected to atomic force microscopy (AFM) to measure the coefficient of friction (COF), i.e., the ratio of the friction force and the applied normal force, on the different surfaces. AFM is a principal tool to study the boundary lubrication phenomena at the molecular level, which occur at high loads and low sliding speeds [49]. Due to the small sizes involved, AFM is a very suitable device to study the phenomena where high local pressures squeeze out the lubricant liquid at the contacting asperities and result in solid–solid contact, while a (mono)layer of lubricant molecules prevents the interpenetration or adhesion at the asperities. The combination of QCM-D and AFM has been used to study the molecular adsorption and biolubrication of the proteinaceous lubricant films [38,50–52].