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Investigation of Effect of Hyaluronic Acid Containing Medicine on Frictional Behavior of Synovial Fluid

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Abstract

Cartilage and synovial fluid ensure the smooth movement of natural joints to work with very little friction. However, the number of patients with joint diseases, which are usually related to cartilage destruction, constantly increases. Therefore, understanding the tribological behavior of synovial fluid is of great concern in order to reduce its degradation and maintain a reliable joint function. The purpose of this research is to provide insight into the frictional behavior of synovial fluid, focusing on its composition and especially hyaluronic acid (HA) content, velocity, and applied load on the joint. For this purpose, a pin-on-disc simulator was used. The tests were accomplished at three different movement velocities and under three loads of 30, 60, and 100N. During the tests, the lubricants were pure synovial fluid and synovial fluid with 10% and 20% of a traditional osteoporosis medicine, i.e. Cynogel. The test results showed that the friction strongly depends on the HA content of the lubricant. Studying the applied load effect on the friction coefficient, it was found that hyaluronic acid's rheological behavior could neutralize the medicine's effect under a light load at a slow speed. After adding Cynogel into the synovial fluid, the friction coefficient decreased under higher loads. The greatest changes were observed for the 20% combination, which led to about 20% and 30% improvement in the friction coefficient at high and medium velocities, respectively.

1. Introduction

Due to joints, the movements of human body parts are very flexible and they have smooth movements. The joint mechanisms are naturally optimized with a minimal friction and protected against wear under different loads and velocity conditions. High wear resistance besides a slight friction is mainly exerted as a result of articular cartilage and its microstructural configuration. The tribology of joints is related to many key factors; therefore, synovial lubrication has greatly interested researchers [1, 2]. To obtain realistic performance of artificial synovial joints, researchers are trying to analyze the lubrication mechanism and frictional characteristics of real joints to modify and implement prosthetic components [3]. The results of the research can be useful for increasing knowledge in the treatment of osteoarthritis, synovial joint replantation, artificial cartilage construction, and synovial diseases.

During the last two decades, a significant number of experiments and hypothetical studies have been reported about lubrication in synovial joints. The results showed that synovial lubrication is a mixed lubrication consisting of synovial fluid film lubrication, synovial fluid macromolecule boundary lubrication, and squeeze

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film lubrication under pressure by cartilage interstitial fluid [4, 5].

Synovial fluid consists of phospholipids, hyaluronic acid (HA), and lubricin. These molecules are ubiquitous in synovial fluid. All three molecules act synergistically and each has a different function to provide superior lubrication on the cartilage surface under high physiological pressures [6]. Apart from the time-dependent friction regulation, macromolecules formed in the synovial fluid, such as proteoglycan lubricin, polysaccharide hyaluronic acid, and phospholipids, form the biological boundary lubrication on the cartilage surface. These macromolecular boundary lubricants facilitate low friction and wear resistance when two opposing cartilage surfaces come into contact. In healthy joints, the solid-solid cartilage contact does not occur. It can be concluded that the extremely low friction and excellent wear resistance of the joint are manipulated by the intervention of the mechanisms of squeeze film and boundary lubrication [7].

HA is a naturally existing substance in synovial fluid. When the joint has arthritis, the HA concentration in the synovial fluid decreases. If the synthetic form of HA is injected into the joint, its viscosity increases, and in this way, the movement of the joint becomes smoother and the pain is reduced. There is insufficient evidence to conclude the usefulness of HA, and it is impossible to comment with certainty on the benefits or harms of this injection [8].

Furmann et al. [9] investigated the synovial fluid composition, velocity, and load effect on the frictional behavior of synovial fluid. Their results showed that protein-based solutions, regardless of the concentration of the components, show almost a similar coefficient of friction. However, the behavior changes significantly with the addition of HA and phospholipids. Berli et al. [10] investigated the knee prosthesis lubrication model, with non-Newtonian fluid and porous rough materials. Their results showed that a larger deformation capacity promotes thick fluid layers despite the surface roughness. Forster et al. [11] studied the effect of loading time on the synovial fluid friction. In a lubrication condition, instead of a complete fluid film, the two-phase cartilage fluid bears a significant amount of load, and the boundary lubrication is governed. Farnham et al. [12] studied the effects of lubricants on the sliding biomechanics of synovial fluid under a physiological load. Their results showed that synovial fluid and HA solutions with a maximum viscosity of saline lubricants were at physiological shear rates of 3^{-10}, and significantly increased lubricant recovery rates during sliding and reduced its amount to a minimum.

Murakami et al. [13] considered the synovial composition's effect on the articular cartilage's tribological behavior. They assessed the frictional changes of healthy and damaged articular cartilage samples against a glass plate lubricated with lubricants containing phospholipid, protein, and HA with a reciprocating wear test apparatus. They also concluded that good tribological condition in healthy synovial joints is due to effective lubrication mechanisms based on the proper combination of articular cartilage and synovial fluid. In another research, Murakami et al. [14] investigated the lubrication of an articular cartilage and an artificial hydrogel cartilage. They found that the superior lubrication performance of healthy natural synovial joints is realized not by a single lubrication mode, but by a synergistic combination of multi-mode mechanisms such as fluid film, two-phase, hydration, gel film, and boundary lubrication. Burris et al. [15] demonstrated the role of slippage and hydrodynamics in joint lubrication. Their results declared that the effect of tribological hydration was more prominent in increasing the velocity, under reduced loads, in the presence of hyaluronic acid, and with increasing the size of the convergence zone. This trend is consistent with the hypothesis that tribological hydration is induced by external hydrodynamic pressure.

Hilser et al. [16] confirmed the synergistic effect of phospholipids and HA in reducing cartilage friction, and they also hypothesized that this effect is because of hydration lubrication. Mederake et al. [17] investigated the effect of three synovial lubricants (sodium chloride, fetal calf serum, and HA) on friction in nine complete carpometacarpal joints of a sheep. Friction in injured joints is significantly increased compared to healthy joints. Comparing different lubricants, the results show the greatest reduction in friction for HA. Rabenda et al. [18] showed a strong relationship between the molecular weight of HA and the rheological properties of its solutions, and they could not find a clear relationship between the molecular weight of HA and the coefficient of friction. Bell et al. [19] showed that HA is an effective boundary lubricant under static conditions and is less effective in dynamic conditions. Some studies recently intend to supplement injection to the joint, and the effect of friction reduction of these medications is investigated [20–22]. The effectiveness of these drugs has not been determined. Some evaluate them as useful and some as ineffective.

Various studies are focused on joint, cartilage, and synovial fluid behavior. However, frictional modeling and evaluation of synovial medication have not been fully understood. Therefore, the present study is designed to provide a specific analysis of the frictional behavior of synovial fluid considering the effect of the combination of synovial fluid and Cynogel (a drug containing the HA compound), entraining velocity, and load. The test conditions were designed based on previous studies to mimic typical daily activities (slow, normal walking, stair climbing - high load). Furthermore, since the synovial fluid composition is supposed to play a key role in synovial lubrication, the focus is on the concentration and mutual interactions of synovial fluid and HA.

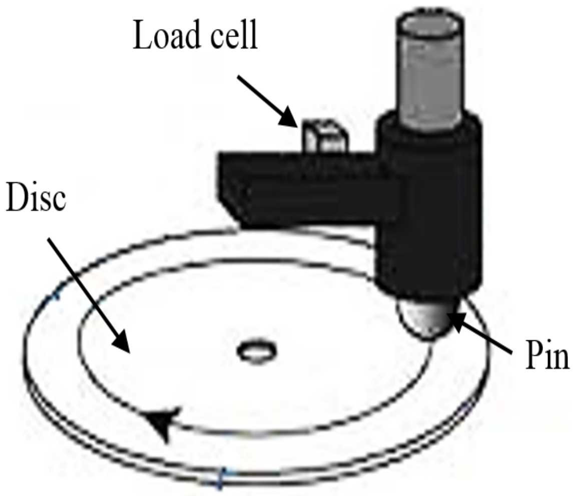

Fig. 1. A view of the pin-on-disc tribometer and the schematic of its operation.

2. Materials and Methods

The pin-on-disc tribometer device shown in Fig. 1 is usually used for investigation of the effect of lubricants on the friction coefficient and the amount of wear under a specific load and velocity according the ASTM G-99 standards. As seen in Fig. 1, in this device, the lubricant is presented between two pieces of disc and pin. The disc rotates at a constant speed, and the pin is loaded on the disc with a certain load. With the help of the load cell device, the friction force between the pin and the disc is measured. The load cell of the device was calibrated with the help of a special weight and the method provided by the device manufacturer. Usually, the pin is made of hard material and the disc is made of softer material, and their surface is polished to the desired roughness. In this study, the 6-mm thick discs were made of St37 steel with a diameter of 90mm, and the pin was made of 52100 steel with a hardness of 64 Rockwell. The discs were polished to a roughness of $< 1\mu$m to ignore the effect of surface roughness on the friction results.

The pin can be placed at three different radial distances of 27, 48, and 66mm from the center of the discs; thus, at a fixed rotational velocity of the device, i.e. 44rpm, three different linear velocities of 0.124, 0.223, and 0.3m/s can be achieved. Fig. 2 shows the disc sample after the test and the path of the pin movement on the disc in this study.

As mentioned earlier, the lubricant used in these tests was prepared from the tapped synovial fluid of patients suffering from osteoarthritis, who were mostly over 60 years old and had been referred to a specialist doctor for aspiration of the knee joint synovial fluid. Cynogel medication (sodium hyaluronate 1.6% with a high molecular weight) was also used to investigate the effect of HA compounds. This drug is available in the form of a ready-made syringe with a concentration of 32mg in a volume of 3ml in the pharmaceutical market. In this research, synovial fluid alone and synovial fluid with the addition of different amounts of 10% and 20% by the volume of Cynogel were used as a lubricant in the tests. Therefore, three different loads, three velocities, and three different lubricant combinations were tested, i.e. a total of 27 tests. To check repeatability and eliminate errors as much as possible, each test was repeated three times. Therefore, in this research, 27 fully polished double-sided discs with the dimensions mentioned above and 27 pins were prepared using ready-made roller bearings. Each disc provides the possibility of 6 tests. The various parameters of the tests performed in this research are given in Table 1.

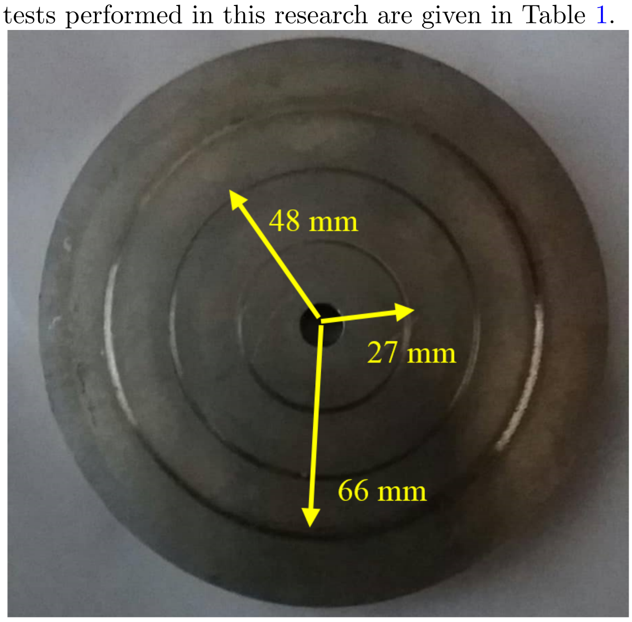

Fig. 2. Disc sample after the test and the positions of pin trajectory.

Table 1
Load, velocity, and lubricant parameters of the designed tests.

Test No.	Load (N)	Medicine (%)	Disc velocity (m/s)
1	30	0	0.124
2	30	10	0.124
3	30	20	0.124
4	30	0	0.223
5	30	10	0.223
6	30	20	0.223
7	30	0	0.300
8	30	10	0.300
9	30	20	0.300
10	30	0	0.124
11	60	10	0.124
12	60	20	0.124
13	60	0	0.223
14	60	10	0.223
15	60	20	0.223
16	60	0	0.300
17	60	10	0.300
18	60	20	0.300
19	100	0	0.124
20	100	10	0.124
21	100	20	0.124
22	100	0	0.223
23	100	10	0.223
24	100	20	0.223
25	100	0	0.300
26	100	10	0.300
27	100	20	0.300

At first, when the pin contacts the polished surface, their roughness interacts with each other, and sometimes they are welded together. After beginning the sliding of the surfaces, the welded roughness pushes and pulls each other which may cause them to break or deform. The change of the roughness, at the beginning of the movement, is called the running-in process. In order to consider running-in, the friction force was measured after a relatively long distance of 200m when the roughness of the surfaces was more smoothened. Therefore, in this way, the possible effect of initial roughness deformation or probable wear was prevented.

3. Results

The pin-on-disc test device measures the friction force during the test time. According to the rotational velocity of the disc and the radius of the pin on it, the distance traveled during the test can be obtained. A sample of the reported data of the friction coefficient by the device for a normal load of 30N at three different velocities is shown in Fig. 3. Also, this figure presents the data for three different combinations of synovial fluid and hyaluronic-containing medicine. The static friction is larger than the dynamic friction. This depends on the nature of the materials in contact: it is a result of some highly complicated phenomena at a microscopic level such as asperity interaction. After the motion, the running-in wear process causes the surface asperity amplitude to decrease. This gradually reduces friction to an asymptomatic value. In lubrication, increasing the velocity forms a thicker fluid layer. As expected, it can be seen in the results that with the increase in velocity, a thicker layer forms, and the possibility of the surface roughness interaction as well as the friction coefficient is significantly reduced. For example, in the case of synovial fluid lubrication, only increasing the velocity from 0.124m/s to 0.223m/s reduced the friction coefficient by 12%. A further increase in the velocity up to 0.3m/s brings this reduction to 55%.

The purpose of this study is to investigate the effect of drugs containing HA. Besides synovial fluid, the combination of 10% and 20% of a famous traditional medicine in the Iranian market (Cynogel) with synovial fluid at different velocities for a specified load of 30N is presented in Fig. 3B and 3C. The reduction in friction with increasing the surface velocity is similar to synovial fluid. In the10% compound, the friction coefficient decreases by 13.8% when the velocity increases from 0.124 to 0.223m/s, and it decreases to 59.4% for the surface velocity of 0.3m/s. In the 20% compound, these reductions are 7% for the surface velocity of 0.223m/s and 53% for 0.3m/s. Therefore, adding HA to synovial fluid under this specific load does not make a significant difference in the reduced friction caused by the increased velocity.

Adding HA under 30N load, for all three mentioned velocities does not affect the friction coefficient significantly. For example, for the synovial fluid lubricant, the average friction coefficient at 0.124m/s is 8% lower than synovial fluid and 10%HA, and 11% higher than synovial fluid and 20%HA. At the velocity of 0.224m/s, these values are 7% lower and 5.8% higher, respectively. At the velocity of 0.3m/s, the friction coefficient for the synovial fluid lubricant is 2% and 8% higher than 10% and 20% HA, respectively. Under this relatively low load, for low and medium velocities, adding the medicine slightly not only reduces the friction coefficient, but somehow increases its value. While the addition of more HA is more efficient.

Fig. 4 shows the changes in friction coefficient for all experiments. Different loads and different velocities and the combination of different lubricants affect the coefficient of friction. Formerly, the changes of friction were described for the light load. However, under higher loads, the trend of change in friction coefficient is similar to each other, i.e. increasing the velocity reduces the friction coefficient. Under a moderate load, the coefficient of friction decreases intensively with increased velocity. Under high loads, the decrease in friction coefficient with the increased velocity has a constant proportionality.

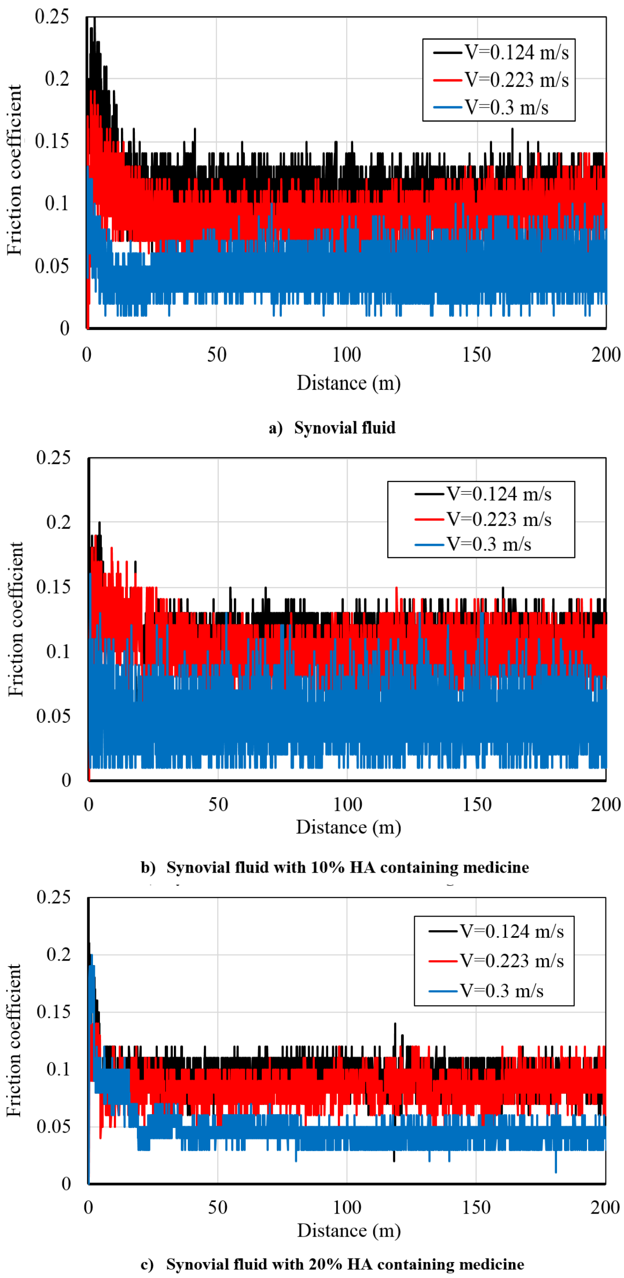

Fig. 3. Changes in friction coefficient for a load of 30N at different velocities for synovial fluid and its combination with a drug-containing HA.

Investigating the effect of lubricant combination or the percentile of medicine used on the friction coefficient under 60 and 100N load shows that even the low-drug content, i.e. 10%, results in a significant decrease in the friction coefficient. This reduction in friction can be seen at different velocities. The reduction rate of the coefficient of friction in the composition of 20% is higher. At 60Nm, adding 10% of the drug-containing HA will decrease the friction coefficient by about 12%, and at 100Nm, about 20% to 35% decrease in friction coefficients can be seen at different speeds. By adding 20% of the drug-containing HA at 60Nm, the friction coefficient decreases by between 25% and 30%, and at 100Nm, this decrease will be between 20% and 30% at different velocities.

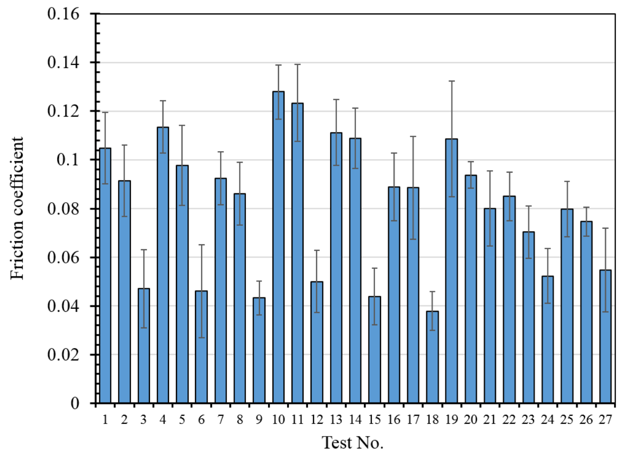

Fig. 4. Friction coefficient variation for various tests.

Synovial fluid is the ultrafiltration of blood plasma (that is, plasma free of large proteins) enriched with locally synthesized polysaccharide molecules called hyaluronan. The hyaluronan molecule in synovial fluid is composed of a very long unbranched, strongly anionic polymer of 25,000 repeating disaccharide units. During loading, which is relatively fast, the hyaluronan chains are randomly connected to each other in the solution; therefore, the response of synovial fluid is quasi-elastic; as a result, the joint can withstand severe loading. On the other hand, under slow and long flow conditions, the chains are forced to align and, consequently, the bonds between them are replaced by water molecules. This results in a partial separation of the hyaluronan chains, leading to their ability to slide past each other more freely, and synovial fluid responds like a shear-thinning viscous fluid. A sharper decrease in the friction coefficient at higher velocities indicates this thin shear property. At small shear rates, the fluid's resistance to movement is high, but with the increase in the shear rate, the fluid becomes more fluent. Therefore, the addition of the material with shear-thinning property can be beneficial against the rapid and large loads that occur during walking and joint activity.

On the other hand, osteoarthritis is a common joint disease characterized by the destruction of articular cartilage and includes changes in the structure and composition of cartilage [4]. The damaged cartilage surface leads to increased friction and causes a slight disruption of the two-phase lubrication mechanism in articular cartilage. HA is a suggested shear-thinning material that shows a beneficial effect on the friction reduction and is very compatible with synovial fluid.

4. Conclusions

Here a challenging problem of using the osteoporosis treatment medicine is considered experimentally using the pin-on-disc simulator. Different compositions of medicine (10% and 20%) and synovial fluid are used as a lubricant. Since all these people had the same disease and were in close age groups, we can more confidently consider the effect of the drug for reduction in the joint friction. The effect of load and velocity is also investigated. The following results are concluded:

- The friction coefficient is reduced with increasing velocity for all types of the lubricant due to improving the lubrication mechanism.
- However, for light load and low velocity, this expectation is not met, and some increase in the friction coefficient is seen with increasing velocity. This is due to the increased viscous friction of the lubricant.
- As the velocity increases, the effect of the viscous friction decreases and the coefficient of friction reduces.
- A higher concentration of HA shows better a tribological condition.
- When 20% of the medicine is compounded with synovial fluid, the friction coefficient reduces drastically with 0 and 10% combination. This demonstrates the importance of using a sufficient dosage of the medicine to have an acceptable response.
- The study limitation is the use of a metallic material for the surfaces while the perfect test should be performed with the same surface materials, i.e., natural joint cartilage. This is due to the fact that it was difficult to make the pin and disk from cartilage, and also the elastic pin caused very high fluctuations in data. However, the results are comparative so they can be generalized to the real situation.

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