DOR: 20.1001.1.27170314.2022.11.4.6.8

Research Paper

Simulation of Drug Release in a Polymer Screw

Amirhossein Badami[1*], Sayed Hasan Mirtalaie[2]
[1]M.Sc. Student, Department of Mechanical Engineering, Najafabad Branch, Islamic Azad University, Najafabad, Iran
[2]Assistant Professor, Department of Mechanical Engineering, Najafabad Branch, Islamic Azad University, Najafabad, Iran
[*]Email of the Corresponding Author: amirbadami.777@gmail.com
Received: December 11, 2022; Accepted: January 27, 2023

Abstract
In recent years, research in the field of pharmaceutical sciences has led to the design of drugs for various diseases. But for the treatment of some diseases, drugs with high side effects and low efficiency are used. Designing targeted drug release systems is one of the solutions to this problem. These systems can deliver a controlled amount of drug to the target cell or tissue. In this paper, drug release was simulated in a screw model designed in Comsol software for orthopedic applications. The purpose of this simulation is to investigate the distribution of the drug concentration on the screw in the surrounding chamber over time. To simulate drug release in a fluid, Navier-Stokes equations for incompressible fluid are used for fluid velocity and pressure, as well as mass transfer equations for the drug concentration distribution. A tetrahedral mesh is used for meshing the model. This simulation is performed in a time-dependent manner for 72 hours with time steps of 0.1 hours. The equations have been solved directly with the PARDISO solver. The obtained results show that drug distribution changes exponentially. As can be seen, the first release of the drug was incremental to 50 hours, and after the release amount, it reached a constant and maximum value.

Keywords
Drug Release, Polymer Screw, Navier-Stokes Equations, Simulation

1. Introduction

Controlled drug release is a process used to ensure the controlled delivery of a drug to the required areas of the body. When a drug is prescribed, the amount must be carefully calculated so that the body can use it. The challenge of new drug treatments is to optimize drug effects and reduce drug toxicity. By carefully controlling the amount or location of the drug in the body, side effects are reduced. Today, investigations are constantly progressing to improve release control agents, so that they can control drugs that have a rapid-release metabolism [1, 2]. In the development of drug delivery systems, most attention has been paid to controlled or slow-release systems to achieve optimal therapeutic effects. Additionally, many systems such as wearable and in combination with machine learning are used for therapeutic effects [3-7].

The design of release systems is usually based on physicochemical properties and drug kinetics [8]. Often, for the drug to be effective in the body, a minimum amount of therapeutic consumption is required. Because most of the conventional systems such as pills have a large amount of consumption

and the result of their consumption can have adverse toxic effects. For the advanced design of systems containing a certain amount of drug, different types of carrier materials have been developed to release the required amount of drug in the desired place in the required time [8,9]. All drugs must have some solubility in water. On the other hand, most of them must be lipophilic to penetrate the biological membrane. In the pharmaceutical industry, cyclodextrins are mainly used as complex forming agents to increase the solubility of drugs with low solubility and to increase the stability of the drug.

The use of nanofibers in drug release systems is of interest to researchers due to the high surface-to-volume ratio and the resulting advances in using them as scaffolds for cell growth and wound healing [10]. Porous nanomaterials are a group of materials that, due to their high surface area and large pore volume, are known as one of the important components for use in drug release systems [11]. Porous materials are classified according to the international unit and according to the size of their holes. The size of holes below 2 nm is called a micro-hole, the size of holes between 2 to 50 nm is called a mesophile, and the size of holes larger than 50 nm is called a macro-hole [12]. Aerogels are synthetic porous materials in which gas replaces the liquid components of the gel. Low density, porosity, and high surface area are important characteristics of these materials [13]. Among all materials with a stable structure that were investigated for drug release, silica materials with a specific structure and surface properties were recognized as biocompatible [14]. For controlled release applications, silica can store and gradually release drugs [15] and among the different methods of preparing nanofibers [16-18], the electrospinning method provides a lot of flexibility in choosing materials for drug release applications, so both of biodegradable and non-degradable materials are used for controlled release. Nowadays, all kinds of drugs such as antibiotics [19], and anticancer agents [19, 20] can be placed inside the electrospun scaffolds [R N A and D N A,] and proteins [21].

In this paper, drug release was simulated in a screw model designed in Comsol software for orthopedic applications. To simulate drug release in a fluid, Navier-Stokes equations for incompressible fluid are used for fluid velocity and pressure, as well as mass transfer equations for the drug concentration distribution. This simulation is performed in a time-dependent manner for 72 hours with time steps of 0.1 hours. The obtained results show that for up to 50 hours, the first release of the drug was incremental and after the release amount reached a constant and maximum value.

2. Material and Methods

2.1 Geometry

The geometry of the model was three-dimensional. The geometry of the screw is designed in Solidworks software and after the design, it is entered into Comsol software. In Fig. 1, the map and three-dimensional design of the screw can be seen. The geometry of the container is a cylinder with a radius of 3 cm and a height of 2 cm. As seen in Fig. 2, 2 cm of the length of the screw is inside the container and the rest is outside.

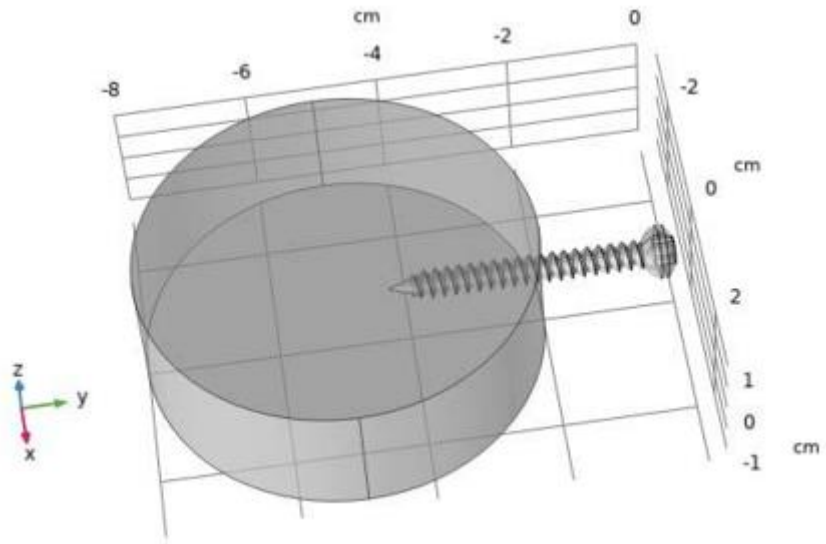

Figure 1. Geometry used in Comsol software

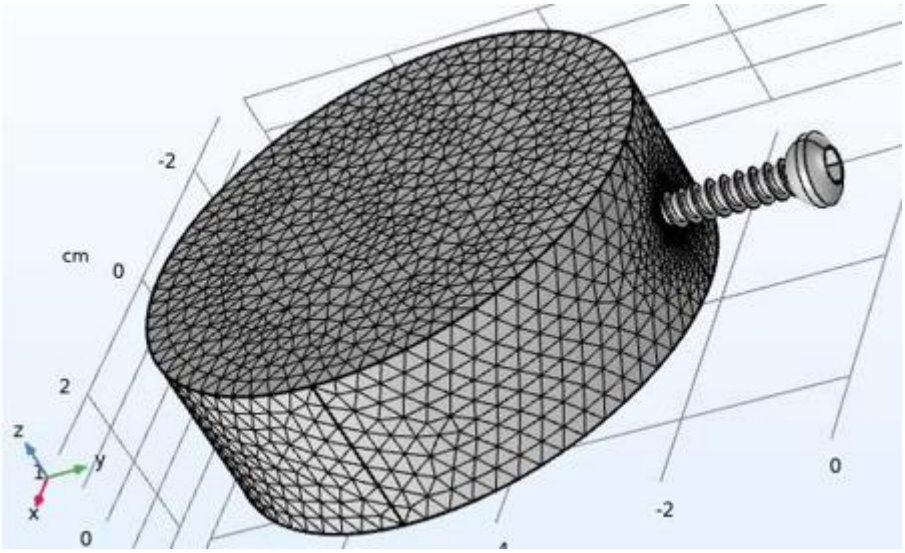

Figure 2. Meshing the model in Comsol software

2.2 Equations

To simulate drug release in a fluid, Navier-Stokes equations for incompressible fluid are used for fluid velocity and pressure, as well as mass transfer equations for the drug concentration distribution. The Navier-Stokes equation is defined as Eq.1:

$$(u + u: Ou) = O + O:T + f \qquad (1)$$

Where is density, u is velocity, t is time, T is shear stress and f is volume forces. The mass transfer equation is also defined as Eq. 2:

$$\frac{c_i}{t} + O:(DOc_i) + u:Oci = 0 \qquad (2)$$

Where ci is the concentration and D is the diffusion coefficient. The continuity equation is also defined as Eq.3.

$$O{:}u = 0 \qquad (3)$$

2.3 Initial and boundary conditions

The initial concentration inside the chamber is assumed to be zero while the initial concentration for the screw is set to Cin. The speed and pressure of the fluid in the entire chamber were equal to zero. No entrance or exit has been considered for the chamber and all the walls have been provided with non-slip conditions and no concentration exchange has taken place.

2.4 Material specifications

The space around the screw in the chamber is considered water and the material of the screw is considered polymer. Table 1 shows the specifications of the materials used in the simulation.

Table 1. Material specifications

Specifications	Amount
water density	1 kg/m^3
viscosity (u)	0.001 pa:s
Drug penetration coefficient in water (D_w)	$3\times10^{11} cm^2/s$
Penetration coefficient of drug in polymer (D_p)	$2.79\times10^{10} cm^2/s$
Porosity percentage (ep)	0.3
Initial concentration (C_i)	3.0342 mol/m^3

2.5 Mesh

A tetrahedral mesh is used for meshing the model. The number of elements in this grid was 89058. The outer part of the screw is not gridded because it is not used in modeling and physics. Fig. 2 shows the form of the model with the grid.

2.6 Solution method

The current simulation is done in the space of Comsol software. This simulation has been done in a time-dependent manner for 72 hours with time steps of 0.1 hours. The equations have been solved directly with the PARDISO solver. The absolute error is considered equal to 0.1. The time required for simulation will take about 15 minutes considering having a system with 32 GB of RAM.

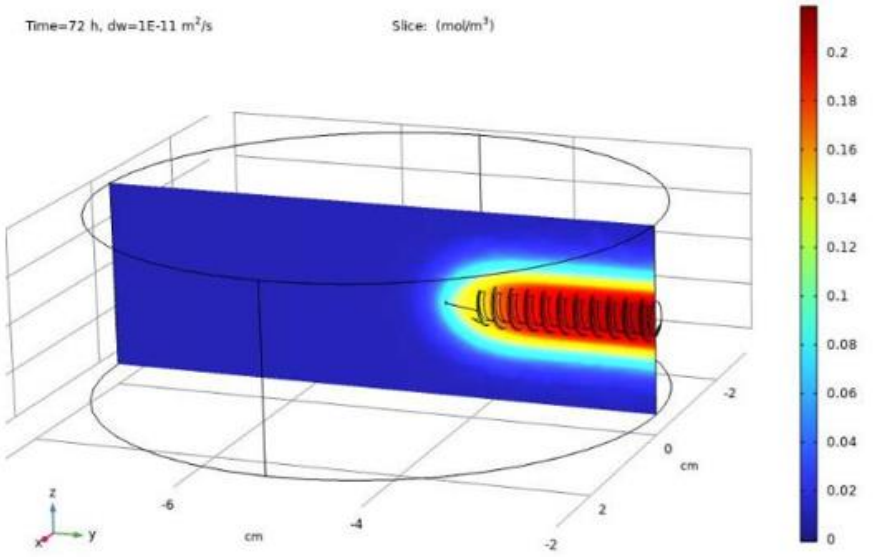

Figure 3. Drug distribution for a diffusion coefficient of $1\times10^{11}cm^2/s$

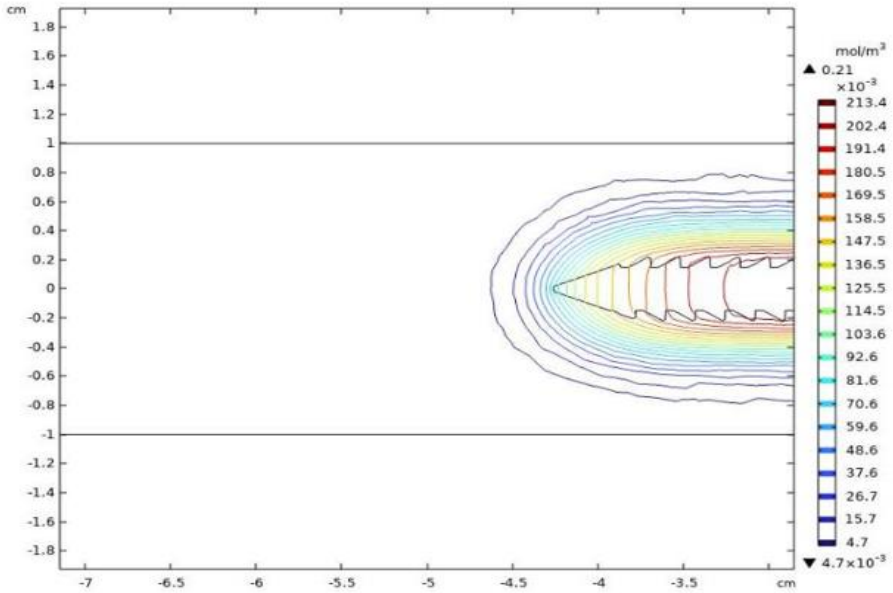

Figure 4. Concentration contours in the model

3. Results and discussion

3.1 Two-dimensional drug distribution

In Figure 3, the drug distribution can be seen on the middle page of the model. As can be seen, after 72 hours from the start of the release, the concentration is observed point by point. The red points are the points that have the highest amount of drug and the blue points are the points that have the lowest amount of drug.

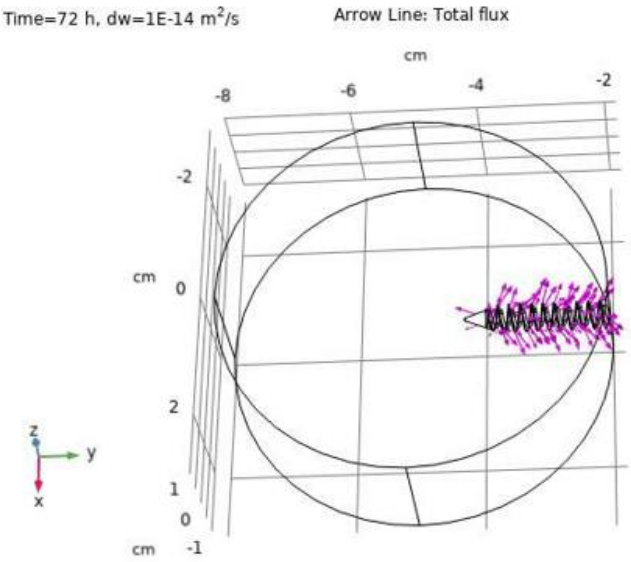

Figure 5. Arrow line display

To better see the drug distribution process from the screw, the drug concentration contours for the diffusion coefficient of E^{-11} cm^2/s are drawn in Fig. 4. Each of these lines represents a concentration in the model. To check the distribution direction of the concentration inside the chamber, the arrow line is drawn as shown in Figure 5.

3.2 Percentage of drug release

In this section, the amount of released drug has been calculated by dividing the total concentration by the initial concentration using integration in the entire chamber. To check the effect of the drug diffusion coefficient in water, this parameter is set as a variable. As can be seen in Figure 6, the way of drug release is different in different penetration coefficients in this period. For example, at a higher diffusion coefficient, the amount of drug release reached equilibrium, while at low diffusion coefficients, the release process has not yet finished. After about 20 hours of the process time, the percentage of drug release in the diffusion coefficient equal to E^{-8} cm^2/s was about twice the model with the diffusion coefficient of E^{-14} cm^2/s.

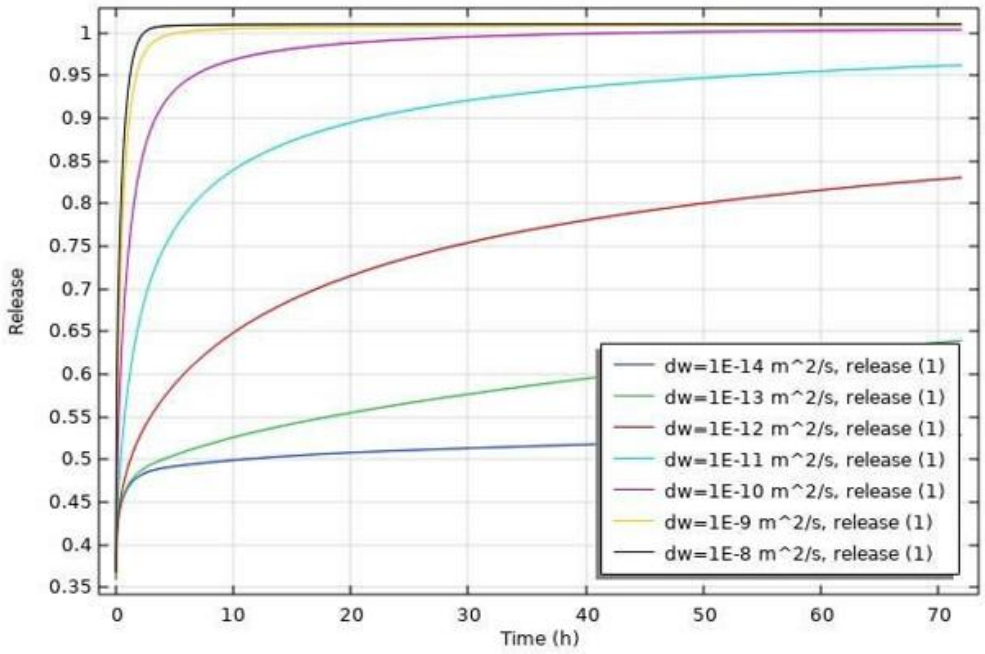

Figure 6. Calculation of drug release in the form of a graph

As it was earlier mentioned, a simulation of drug release in a polymer screw is investigated in this paper. However, the attention of researchers has been attracted to various methods for drug loading in nanofibers, such as coating [19], drug embedding [19], and drug encapsulation (coaxial electrophoresis and emulsion) [19]. The main advantage of fibrous carriers is that the release of drugs is performed by them into the body at a specific location. Also, more than one drug can be directly inside the capsule fibers.

In another case of drug release [22], silk fibroin, as a natural polymer, is widely used in the form of a suitable matrix in controlled drug release systems. Silk fibroin is a biocompatible polymer with slow degradability that has excellent mechanical properties and process ability. In their research, a cyclodextrin scaffold with molecular trapping capability was prepared from a new β-nanofiber from silk fibroin containing cyclodextrin in the formic acid solvent, and the effect of β-electrospinning of homogenous solutions of fibroin and the presence of cyclodextrin on the properties of the produced nanofibers and the amount of drug release was investigated [22]. The morphology, microscopic structure, chemical composition, and thermal behavior of this nanofibrous scaffold composition were investigated by FTIR, SEM, and DSC. Their results of the images showed that the nanofibers were prepared without grains and were uniform, and the average diameter of the nanofibers was influenced by the mixture ratio so that the diameter of the fibers decreased with the increase in the amount of β-cyclodextrin [22]. In another research, mesoporous magnesium silicate was produced with the help of p123 non-ionic surfactant and by sol-gel method [23]. Magnesium silicate was produced in an acidic environment and subjected to calcination at 550 degrees Celsius to remove organic substances. This research aims to investigate the ability and application of controlled loading and release of ibuprofen from mesoporous magnesium silicate composition. Also, the effect of drug loading and release on surface properties such as surface area, pore size and volume, and pore order were evaluated and mesoporous magnesium silicate can load and release ibuprofen and can be used as a new drug delivery system [23].

4. Conclusions

In this paper, drug release was performed in a screw model designed for orthopedic applications. The purpose of this simulation is to investigate the distribution of the drug concentration on the screw in the surrounding chamber over time. First, the screw is simulated in Comsol software, and then this screw is placed in a cylindrical chamber with a radius of 3 cm and a height of 2 cm. The obtained results show that initially, the amount of drug near the screw is extremely high, while this amount is less in this area far from the screw. Over time, the amount of medicine around the screw decreases and penetrates more into the chamber and finally reaches a maximum value and saturation.

5. References

[1] Santadkha, T., Skolpap, W. and Thitapakorn, V. 2022. Diffusion Modeling and In Vitro Release Kinetics Studies of Curcumin−Loaded Superparamagnetic Nanomicelles in Cancer Drug Delivery System. Journal of Pharmaceutical Sciences. 111(6): 1690-1699.

[2] Yadav, M., Thakore, S. and Jadeja, R. 2022. A review on remediation technologies using functionalized cyclodextrin. Environmental Science and Pollution Research. 29(1): 236-250.

[3] Abbasi-Kesbi, R. and Nikfarjam, A., 2017. Denoising MEMS accelerometer sensors based on L2-norm total variation algorithm. Electronics Letters. 53(5): 322-324.

[4] Fathi, M., Nemati, M., Mohammadi, S.M. and Abbasi-Kesbi, R. 2020. A machine learning approach based on SVM for classification of liver diseases. Biomedical Engineering: Applications, Basis and Communications. 32(03):2050018.

[5] Abbasi-Kesbi, R., Memarzadeh-Tehran, H. and Deen, M.J. 2017. Technique to estimate human reaction time based on visual perception. Healthcare technology letters. 4(2): 73-77.

[6] Akhavanhezaveh, A. and Abbasi-Kesbi, R. 2021. Diagnosing gait disorders based on angular variations of knee and ankle joints utilizing a developed wearable motion sensor. Healthcare Technology Letters. 8(5): 118-127.

[7] Abbasi-Kesbi, R., Asadi, Z. and Nikfarjam, A. 2020. Developing a wireless sensor network based on a proposed algorithm for healthcare purposes. Biomedical engineering letters. 10(1): 163-170.

[8] Machín, R., Isasi, J.R. and Vélaz, I. 2012. β-Cyclodextrin hydrogels as potential drug delivery systems. Carbohydrate polymers. 87(3): 2024-2030.

[9] Del Valle, E.M. 2004. Cyclodextrins and their uses: a review. Process biochemistry. 39(9): 1033-1046.

[10] Bhardwaj, N. and Kundu, S.C. 2010. Electrospinning: a fascinating fiber fabrication technique. Biotechnology advances. 28(3): 325-347.

[11] Arruebo, M., 2012. Drug delivery from structured porous inorganic materials. Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology. 4(1): 16-30.

[12] Davis, M.E. 2002. Ordered porous materials for emerging applications. Nature. 417(6891): 813-821.

[13] Zhang, X., Liu, K., Zhao, J., Zhang, Z., Luo, Z., Guo, Y., Zhang, H., Wang, Y., Bai, R., Zhao, D. and Yang, X. 2022. Mechanically interlocked aerogels with densely rotaxanated backbones. Journal of the American Chemical Society. 144(25): 11434-11443.

[14] Graf, C., Dembski, S., Hofmann, A. and Rühl, E. 2006. A general method for the controlled embedding of nanoparticles in silica colloids. Langmuir. 22(13): 5604-5610.

[15] Götz, W., Tobiasch, E., Witzleben, S. and Schulze, M. 2019. Effects of silicon compounds on biomineralization, osteogenesis, and hard tissue formation. Pharmaceutics. 11(3): 117.

[16] Khalil, A.M., Hassanin, A.H., El-kaliuoby, M., Omran, N., Gamal, M., El-Khatib, A., Kandas, I. and Shehata, N. 2022. Innovative antibacterial electrospun nanofibers mats depending on piezoelectric generation. Scientific Reports. 12(1): 1-15.

[17] Hebatalrahman, A., 2022. An Investigation of the Manufacturing Process, Structure, and Performance of the new micro and mano thermoplastic-based composites prepared with zeolite filler. Journal of Modern Processes in Manufacturing and Production, 11(1): 5-19.

[18] Haghshenas, A. and Shahrajabian, H. 2021. The mechanical properties of PA6/NBR/clay/CaCO3 hybrid nanocomposites. Journal of Modern Processes in Manufacturing and Production. 10(1): 19-30.

[19] Melchor-Martínez, E.M., Torres Castillo, N.E., Macias-Garbett, R., Lucero-Saucedo, S.L., Parra-Saldívar, R. and Sosa-Hernández, J.E. 2021. Modern world applications for nano-bio materials: tissue engineering and COVID-19. Frontiers in Bioengineering and Biotechnology. 9:597958.

[20] Xu, X., Chen, X., Xu, X., Lu, T., Wang, X., Yang, L. and Jing, X. 2006. BCNU-loaded PEG–PLLA ultrafine fibers and their in vitro antitumor activity against Glioma C6 cells. Journal of controlled release. 114(3): 307-316.

[21] Fan, S., Zhang, Y., Huang, X., Geng, L., Shao, H., Hu, X. and Zhang, Y. 2019. Silk materials for medical, electronic and optical applications. Science China Technological Sciences. 62(6): 903-918.

[22] Nouri, M., Mokhtari, J., Salmani, L. and Sadeghieh, K. 2016. Electrospinning of Silk Fibroin/-Cyclodextrin Nano bers for Controlled Drug Release. Iran. J. Polym. Sci. Technol. 29: 89-100

[23] Bigham, A., Hassnzadeh, T.S.A., Rafienia, A. and Salehi, H. 2018. Synthesis and characterization of mesoporous magnesium silicate for controlled release drug applications. Journal of Advanced Processes in Materials Engineering. 12(1):73-83.