PLURONIC F127: RHEOLOGICAL STUDY WITH DESIGNING AND SIMULATING A SYRINGE FOR DRUG DELIVERY SYSTEMS

Laboratory and simulation assessment

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Abstract

The hydrogels are getting a lot of interests in the modern days in terms of their effectivity in drug delivery systems. The hydrogels are controllable and flexible in terms of their concentration and composition to be used as therapeutic drugs, where their main application field refers to the biomedical applications in healthcare. Recently, drug delivery systems that are based on hydrogels usage are being tested in laboratories to be able to address cell transplantation for cancer curation. Therefore, the composition of the hydrogels based on their viscoelastic properties is critical and have to be optimised along with the drug delivery system used. Therefore, in this project, Pluronic F127 hydrogel is tested to withdraw its main rheological features along with a design and analysis of the required drug delivery system for injection purposes. The Pluronic F127 viscosity increases with the decrease of the shear rates along with an increase in viscosity with the increase in concentration. This variation refers to the molecular mass variation from the ratio of PEO-PPO-PEO triblock copolymer composition. The pressure drop also decreased with the increase of the shear rates for concentrations of Pluronic F127 higher than 25%. The design of a syringe capable to deliver the Pluronic F127 at room temperature is simulated in SolidWorks with a flow rate of 10000μL/min and a temperature of 20℃. The sol-gel transition of this Pluronic F127 occurs at 29℃ which shows its viability in application.

Acknowledgment

First, I would like to Thank Prof Tim Gough for directing me in the right direction and providing the required data for the finalising of the project. Also, I would like to Thank all my close family for being next to me mentally and totally supportive in these hard times. The Covid-19 situation affected me in a huge way, where I lacked concentration and definitive work generation, however, with the support I was given from the family and the reassurance from the University, I competed this project.

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1 INTRODUCTION

Drug delivery systems are emerging in recent studies based on their ability to cure several health issues in a cost effective and advanced way. The design analysis of drug delivery systems mainly focuses on the usage of hydrogels referring to their advantages in being stable therapeutic systems. The hydrogels have various specifications that are discussed later in the research executed in this project, where they have the upper hand over the conventional therapeutic drug delivery systems referring to the ease in their usage and stability (Qureshi, et al., 2019). The hydrogels are relying on the polymer networks, where these polymers have hydrophilic feature. The hydrophilic feature refers to the affinity against water-based solutions. In addition, the hydrophilic polymers had raised interest in research in terms of the biological systems based on their superior colloidal properties. These features make the hydrophilic polymers creating the hydrogels drug delivery systems allow them to be suitable for bulky drugs as well. It was reported in (Dubey, et al., 2018) that these products are applied to generate chemotherapeutics drugs and proteins. The first highlight of these polymeric hydrogels refers to their injectability in the human body being biodegradable and easily implemented. This phenomenon creates a convenient approach for doctors and their patients being painless and have less recovery time than the conventional method application. In certain surgeries, bones might be defected and have irregular shapes, where the proposed hydrogel drug delivery systems relying on polymers allows the filling of these irregular spaces. It was reported in (Utech & Boccaccini, 2016) that the hydrogels used in these drug delivery systems are extensively used in bone tissue engineering. In order to understand the overall

composition of these hydrogels and their applications, Figure 1.1 is plotted in the following.

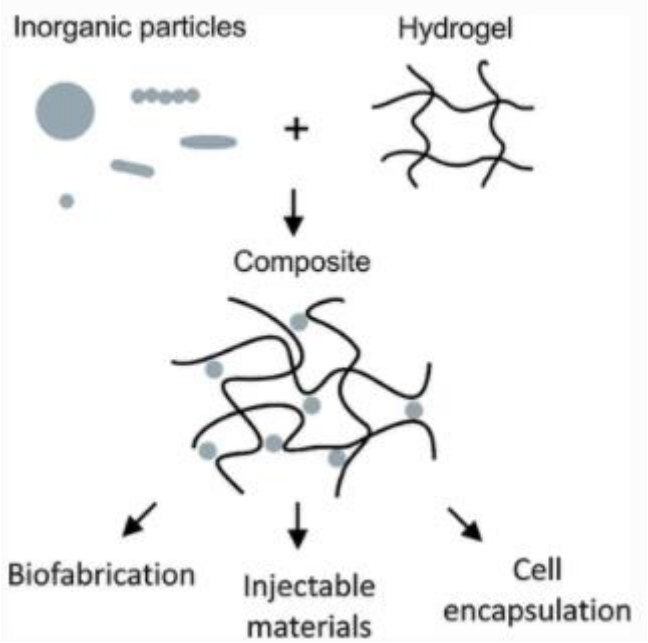

Figure 1.1: Creating composite from hydrogels towards injectable materials (Utech & Boccaccini, 2016).

There are various hydrogels to be used in the bone tissue repairs in other drug-based surgeries. Therefore, the hydrogels are categorised in terms of injectable biomaterials, where the main focus is assessed on their hydrophilic polymers. It was reported in (Boonlani, et al., 2018) that the composites illustrated in Figure 1.1 should be altered in terms of cross-linking in order to result in insoluble polymer. Following the discussed information on the drug delivery systems, where their injectability is approached in terms of the advantages in tumour healing and optimise the dosage in drugs. However, in clinical approaches in hospitals have a preferability towards direct injection in order to assess the invasively conventional methods. It was reported in (Fattah & Mansour, 2018) that the improvement in tissue engineering refers to the cell injection, where the drug delivery systems optimises this application.

Several studies showed interests in cell injection in terms of the viability that focuses on the host environment in the human body, where the effect of these cells injectability should be monitored in terms of the immune response as reported in (Shrestha, et al., 2020). In the conventional approaches, the injection protocols were applied based on trial and error. The trial and error mainly focus on the doctors and surgeons experience, where the current approaches are replacing the trial and error to increase the accuracy of dosage and toxicity in cell injection. The delivery modules mentioned in the studies are assessed based on the typical doses to accelerate and improve the modalities in cell transplantations. These typical doses refer to the sustainable release that should be applied in a controlled environment which is assessed in a biodistribution assessment. It was reported in a study by (Chen, et al., 2016) that the formation of 3D networks in hydrogels are assessed in situ formation referring to the resultant hydrogels. These hydrogels result in loading that is assessed as follows:

1) Water soluble drug generation.
2) Insoluble in water drug generation.

The aforementioned information on drug delivery systems and the conventional ways are not set to be limited to the traditional ways to generate chemical therapeutic compounds. However, these described ways have to result in the generation of chemical compounds, such as, proteins, cell injection, therapeutic drug delivery, etc. It should be noted that the usage of drug delivery systems is referred to the design of the actual mechanism. However, in a specific aspect of the injectable hydrogels they are referred to the external stimuli; hence, the environment of the injectability should be assessed in terms of its reversibility.

1.1 AIM

The aim of this project is to study the rheological properties of the Pluronic F127 hydrogel for potential application in drug delivery system. A design of a syringe is required in order to assess the behaviour of the F127 hydrogel during injection based on the variation of its concentration, shear rates, and the temperature range applied.

1.2 OBJECTIVES

the objectives of the project are:

1) generate a literature review on hydrogels and their usage and applications in biomedical and healthcare field.
2) Discuss the main features of the hydrogels to withdraw their specifications and rheological aspects.
3) Generate the methodology of the results analysis and the design steps for the syringe.
4) Assess the design and create the intended syringe on SolidWorks with mentioning the required assumptions.
5) Analyse the flow of the Pluronic F127 on SolidWorks software and compare the results with the analytical solution of the pressure calculation.

1.3 PROJECT STRUCTURE

This current project has 6 coherent chapters, where the first and the current one has the background information on hydrogels and their importance in drug delivery systems. Also, this chapter illustrates the aim and objectives of the project with its structure. The second chapter is the literature review on the hydrogels type and their applications. The third chapter illustrates the steps to analysis the data collected from

the laboratory along with the steps to design the syringe for injection purposes of the Pluronic F127. The fourth chapter presents the results generated from the analysed data to study the visco elastic features of the Pluronic F127. The fifth chapter presents the discussion in terms of the main aspects of the analysed data. Finally, the sixth and the last chapter denotes the withdrawn conclusions and future work.

1.4 SUSTAINABILITY AND ETHICS

The sustainability of this projects is assessed in terms of the cost-effective measure provided by the hydrogels application in drug delivery systems. Their application is sustainable in terms of their avaialb0lity as biomass like cellulose, which decreases costs dramatically in comparison with the conventional ways of therapeutic surgeries and drug delivery. Another aspect of sustainability is the simulation of these hydrogels on SolidWorks, which reduce costs of machinery used to analyse these flow and remove trial and error in optimizing the aspects of the application, such as, the syringe design and the viscoelastic computability of the hydrogel used. In terms of the ethics, all resources were referenced along with mentioning that the laboratory data was acquired from Prof. Tim Gough.

2 LITERATURE REVIEW

2.1 INTRODUCTION

In this chapter of the project a research is undertaken on the polymeric gels used in drug delivery systems. The literature assesses the hydrogels with their types with focusing on the tri-block copolymers as they have shown potential in drug delivery systems usage.

2.2 HYDROGEL TYPES AND APPLICATIONS

A broad perspective was assessed on the hydrogels in the interoductory chapter of the report. Hence, the hydrogels are categorized as a special type of polymers with presenting advantages on the high level of water absorption. They could be modified as they are man-made and naturally aspirated. The manipulation of the hydrogels is applied in terms of the alteration of their mechanical and thermal properties to be optimised within their application in healthcare applications and mainly drug delivery systems (Mishra, 2015). Recent studies have reported that the hydrogels have high potential in terms of cell transportation techniques, where they allow the cell injections based on the Matrigel. Matrigel were reported as complex hydrogels to optimise the cell transplantation and they are mainly relying on laminin in their composition (Tessmar, et al., 2017). The Matrigel is manipulated from the naturally aspirated product generated from the mouse sarcoma cells. The manipulation of such hydrogel allows its biocompatibility in terms of the application in humans to target certain tissues or organs. It should be noted that the monitoring of the effect of these hydrogels takes place in the post delivery aspect. It was reported in (Park, et al., 2011) that the hydrogels are used in scaffolds as well. This type of application interfere within the

creation of scaffolds that support the bone construct of humans of their tissues. The scaffolds application helps in increasing the controllability and flexibility in tissue growth. Moreover, the encapsulated cells are protected by the hydrogels as they minimise the risks of local inflammation. It should be noted that the hydrogels are categorized in different types referring to the medium they applied in, along with the effectivity of such medium on their properties. The following critically discuss their application and criteria.

2.2.1 Temperature sensitive

The first hydrogel type to be discussed in this section refers to the temperature sensitive hydrogels. They are named as temperature sensitive hydrogels based on their effect on the temperature variation of their medium. The temperature variation of these hydrogels refers to the phase separation occurring at the hydrogel level between the rich and lean phase as reported in (Hunyh & Lee, 2012). The assessed parameter in temperature sensitive hydrogels refers to the critical solution temperature abbreviated as CST. The CST illustrates the critical temperature that varies the polymer from the hydrophilic to the hydrophobic phase. This phase variation refers to the interaction occurrence between the complex polymer chains. Hence, Figure 2.2 illustrates the volume fraction variation in the polymer chains based on the temperature variation.

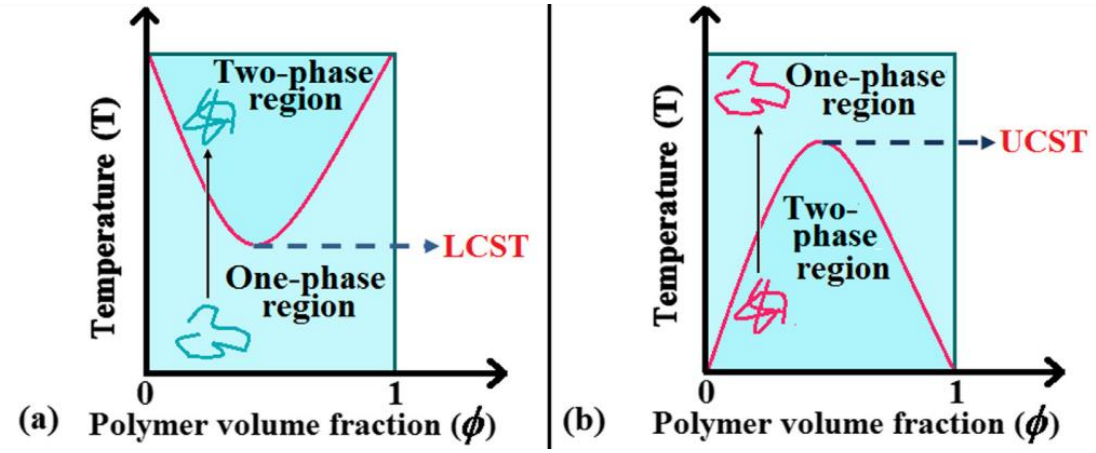

Figure 2.1: Polymer volume fraction variation based on temperature change (Hunyh & Lee, 2012).

It should be noted that the temperature variation is assessed based on the CST as illustrated in Figure 2.1. Referring to the diagram above, it was noted that there are two CSTs explained in Table 2.1 and was reported in (Qureshi, et al., 2019).

Table 2.1:Critical solution temperature explanation based on the lower and upper aspects.

Critical solution temperature	Description
Lower critical solution temperature	Lowest point in the phase transition diagram that denotes the solubility of the polymer.
Upper critical solution temperature	Highest point in the phase transition diagram that denotes the biphasic aspect of the polymer.

It was reported in another study by (Zhang, et al., 2005) that the hydrogels respond to the temperature variations, which their name are derived from. Hence, these hydrogels are fabricated based on cross linking of the solution. In addition, these hydrogels face a phenomenon called sol-gel transition, where this phenomenon is induced by temperature variation. The phase transition of sol-gel is applied to attain the required

LCST. In order to emphasise on the sol-gel transition, several polymers are investigated upon their transition temperature. The polymers are illustrated in Table 2.2 along with their transition temperature and the type of CST the transition occurs at.

Table 2.2: Polymers with their transition temperatures.

Polymer name	Type	Transition temperature
Polyacrylamide	UCST	25
Poly(methyl vinyl ether) (PMVE)	LCST	37
Poly(N-ethyl acrylamide)	LCST	74

Following the description and analysis of the temperature sensitive hydrogels, several studies considered them as an essential drug delivery system. Such selection refers to the safe cell encapsulation that can include the release of several agents mainly used in tissue therapy (Das, 2018). It was reported in (Wang, et al., 2013) that Pluronics are considered as thermosensitive hydrogels that are modified to be biodegradable and used in drug delivery systems to fix major organ and tissue problems. The hydrogels used in the human body must be biodegradable in order to minimise the risk of any inflammation upon their application. Another study by (Varaprased, et al., 2012) reported the usage of a thermo sensitive polymer called F127 that was included in a complex structure set as a copolymer of the composition plotted below:

poly(trimethylene-carbonate)15-F127-poly(trimethylene-carbonate)15 (PTMC15-F127-PTMC15)

The study revealed and concluded that the usage of such copolymer showed efficiency mechanical properties with high biocompatibility in order to be used in drug delivery systems.

2.2.2 Photo-sensitive

Following the temperature sensitive hydrogels, the type addressed in this section refers to the photo-sensitive hydrogels. This type of hydrogels is assessed in the literature based on the high accuracy in localization in the post-delivery monitoring. In addition, these hydrogels were reported as reversible, which means that they can undergo chemical and physical alteration of their properties (Munim & Raza, 2019). The modification is applied based on exposing them to the light. Figure 2.2 illustrates the light exposure on the polymeric hydrogels. However, it should be noted that few studies have applied this type of hydrogels as they are undergoing further research and investigation for safe and beneficial usage in healthcare applications. The biomedical applications of these polymers is addressed in the following points.

1) High controllability in the drug delivery system known as photomediate delivery.
2) Allowing 4 dimensional cell culture, which helps in addressing the dynamicity of the cultured environment.

The physical properties of the hydrogels to be investigated in researched studies focused on their shape, stiffness, degradation rate, and the increment in size upon application. However, for the chemical properties, the researchers focused in the ratio of hydrophilicity to the hydrophobicity. The ratio is assessed during the manipulation of their chemical properties through light exposure as illustrated in Figure 2.2.

(such as surface hydrophilicity/hydrophobicity ratio) of the light-sensitive hydrogels can be fine-tuned by merely modifying parameters like light intensity, wavelength, duration of exposure, and type of the photosensitive moieties (Yoon & Kim, 2017). Figure 2.2 illustrates the approach for the hydrogel formation upon photosensitivity consideration.

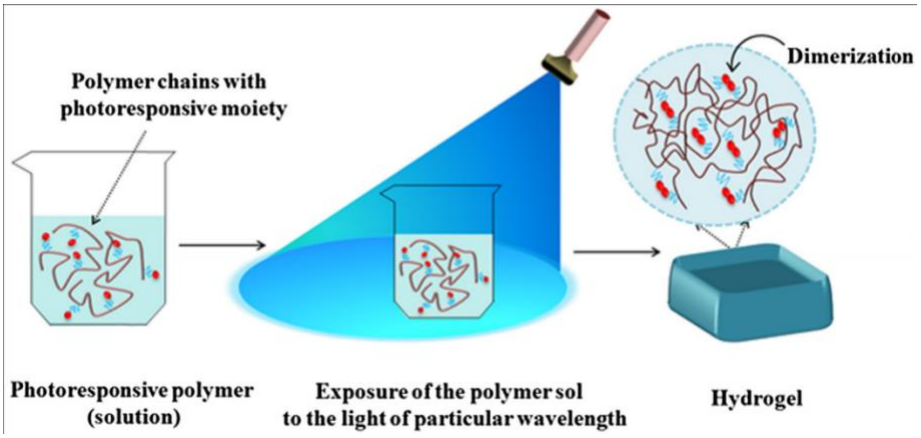

Figure 2.2: Exposure of the polymer to the light at a specific wavelength (Qureshi, et al., 2019).

It should be noted that the manipulation requires the variation of the light properties, such as, the wavelength, the intensity, and the time of exposure (Yoon & Kim, 2017). These hydrogels were mentioned in terms of the cell culture as well in (Yoon & Kim, 2017) and (Wang, et al., 2013).

2.2.3 Magnetic field sensitive

The third type of the hydrogel polymers refer to the magnetic field hydrogels, where they are modified and manipulated through the application of a magnetic field. It was reported in (Eid & Mansour, 2013) that there are various material types in terms of such application, such as, organometallic copolymers that are known as nanomagnetic materials. Such type of products have been a centre of interest in magnetic field sensitive hydrogels based on their physical and chemical properties. The magnetic field sensitive hydrogels are considered in studies based on their

polymer matrix softness. The polymer matrix is filled with water and certain magnetic particles selected upon the intended application. Upon the application of a magnetic field on the altered polymer matrix, a deformation occurs on the hydrogel level. It was reported in (Ngadanoye, et al., 2011) that these hydrogels are explored in being applied in biomedical applications, such as, drug delivery systems, and absorbents. Another study by (Li, et al., 2012) reported that the magnetic sensitive hydrogels were a centre of interest in drugs based on cancer curing through the polymerization method.

2.2.4 Shear stress sensitive

Another important type of hydrogels refer to the shear stress sensitive ones, where this refers to the physical properties tuning required in drug delivery systems. A study by (Angar & Aliouche, 2016) reported that polymers could be manipulated referring to their chemical composition based on the application of forces that are illustrated in shear and strain occurrence. The transformation of the polymers under certain forces is called mechanical induction, where the polymer chains are targeted to vary the covalent bonds related to the chemical properties. Furthermore, it was reported in (Li & Mulay, 2011) that the hydrogels undergo variations based on the changes in their mechanical properties, such as, stress and strain. Therefore, they are known as shear stress sensitive polymers. Towards more technical and in-depth understanding of the mechanical properties' variation of these polymers, they have to demonstrate a variation on the viscosity level which has a direct effect on the shear stress occurrence. The viscosity variation refers to the viscoelastic property of the polymer under study, where it might undergo two different phenomenon (Li & Mulay, 2011) described in Table 2.3.

Table 2.3: Viscoelastic phenomenon description for shear stress sensitive hydrogels.

Viscoelastic phenomenon	Description
Shear thickening	The viscosity of the hydrogel increases following the shear application.
Shear thinning	The viscosity of the hydrogel decreases following the shear application.

The shear stress sensitive hydrogels have taken a lot of interest in terms of in-situ injectable polymers. Their properties allow them to sustain the drug release at different rates. Mainly, these hydrogels are used in syringe-based drug delivery systems, where they are extruded from these systems. The extrusion of the hydrogels from these systems should be assessed based on the applied load and the shear occurring on the internal walls of the syringe (Khan, et al., 2017). These polymers have taken a centre of interest in biomedical application in order to inject drugs at specific dosage in the human body. The injection and preparation mechanism is illustrated in Figure 2.3. In terms of the viscoelastic phenomenon of shear thinning allows the delivery of the drugs in high rates, where the post-delivery injection should be monitored. It was reported in (Ali & Shah, 2020) that the shear thinning upon injection allows the stabilisation of the network based on the covalent crosslinking. Several studies emphasised on the production of different type of copolymers to be used in the drug delivery systems, where a study generated a glycol chitosan Pluronic (F127) to be used in such application. Promising results were generated in terms of delivery mode and loss and storage modulus based on the viscosity variation.

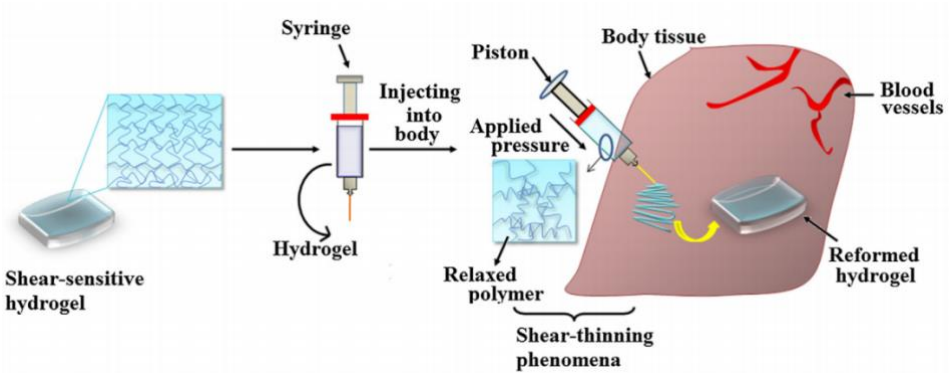

Figure 2.3: injectability of shear stress sensitive copolymers.

Another study mentioned similar approach for the injection of shear sensitive hydrogels on a local tumour based on cancer treated agent. However, the optimal conditions of the mixing were attributed to the Pluronic F127-based copolymer (Zhou, et al., 2014).

2.3 CHITOSAN POLYMERS

In section 2.2 of the literature, chitosan polymers and Pluronic copolymers were mentioned to be used in drug delivery systems. Therefore, in this section, the composition and usage of such polymers are investigated. The chitosan is known as a cationic polymer formulated from the deacetylation of chitin. Such material is find extensively as it illustrates the second most available biomass. The first available biomass naturally aspirated is the cellulose. The chitin could be found in protein-based bodies, such as, shrimp, insects, etc. Chitosan is based on chitin that could be also found extensively in mushrooms as reported in (Wu & Lee, 2017). It should be noted that there are two different types of such hydrogels, where the first one refers to the physical hydrogels. However, the second one relies on the chemical hydrogels. In order to result in a usable chitosan-based hydrogen, it should be chemically altered, where the chemical cross linking bonds should be applied. There are various ways to reach that stage of the cross linking of the bonds. It was reported in (Sampath, et al.,

2017) that genipin could be used as a cross linking agents. The composition of the chitosan hydrogel is illustrated in Figure 2.4. It should be noted that the usage of chemical agents for the cross linking application is critical as not all of the chemical agents are biocompatible.

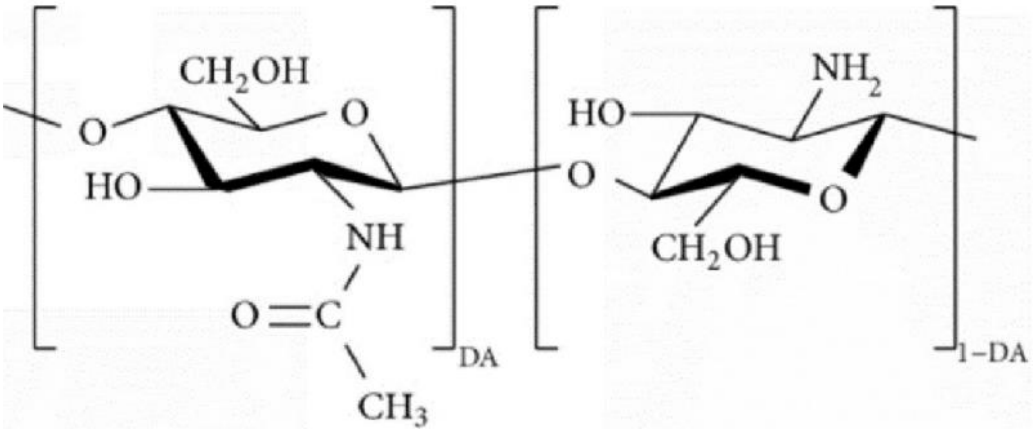

Figure 2.4: Chitosan hydrogel chemical composition (Wu & Lee, 2017).

The selection of the genipin for the cross linking application for chitosan hydrogen creation is based on the assessment of the density required. It was reported that the density is a major factor in hydrogels based on the degradation rate. In addition, the degradation rate has an effect on the mechanical properties of the generated chitosan hydrogel. It was reported in (Bi, et al., 2019) that the bonding name is Van der Waals. The bonding mechanisms refers to the electrostatic interactions, where these interactions occur only on the polymers having high molecular weight (Bi, et al., 2019).

2.4 TRI-BLOCK COPOLYMER F127

In this section, the copolymers used in drug delivery systems are assessed based on their applicability and properties. These copolymers are known as hydrophobic blocks along with hydrophilic blocks, where they are synthesised following critical chemically assessed approaches. It was reported that the most common used block copolymer is the Poly(ethylene glycol) based on its biocompatibility and controllability in

applications. Figure 2.5 illustrates the different available block copolymer used in researched studies and generated by specific companies of biomedical applications.

Figure 2.5: Copolymer types.

The structure of the block copolymers vary based on their chemical generation and their intended application, where it was reported in (Hunyh & Lee, 2012) that ABA and BAB structures are available. The addition of functional groups to the block copolymer refers to the engagement in more applications, which are illustrated in carrying and monitoring behaviour. Furthermore, the addition of functional groups increases the ability for cell penetration for cell transplantation and other applications in healthcare and advanced surgeries usage. The triblock copolymers are assessed in terms of the ability to divide them into symmetrical and asymmetrical copolymers. The structure ABA or BAB is coded following the property or function of the intended copolymer as described in Table 2.4.

Table 2.4: Coded structure description of the copolymer

Coded structure	Function
A	Hydrophobic copolymer
B	Hydrophilic copolymer

In terms of the asymmetric triblock copolymers, they have the ABC structure, which means that the polymers are different and distinctive from each other. The selection of the ABA, BAB, and ABC structure depends on the application of the copolymer.

Figure 2.6 illustrates the different types of copolymers along with their micelle's illustration.

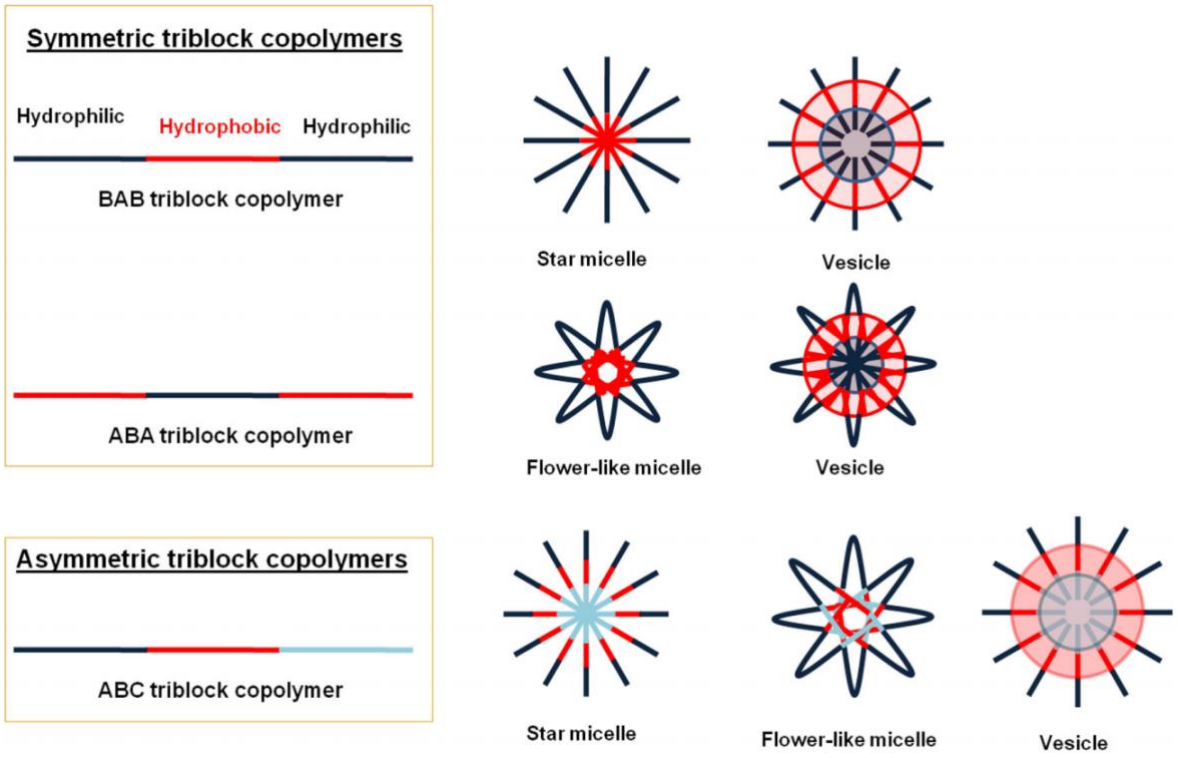

Figure 2.6: Different types of copolymers with their micelle's illustration (Hoang, et al., 2017).

The main challenge in triblock copolymer usage refers to the gene transition referring to the degradation rate that occurs during the application. Several studies mentioned the usage of ABC structured copolymers in gene carrying with validating their stability. Towards more applicability in drug delivery systems, a study by (Samanta & Roccatano, 2013) reported that the usage of PEO-PPO-PEO triblock copolymer showed interesting results in terms of the drug delivery based on the aqueous environment behaviour. In the same study, the Pluronic P85 was assessed with proving high stability in drug placed in water. In order to summarise the property of the Pluronic copolymer, they have multidrug resistance which allow them to be applied in drug delivery systems, where they are defined under the scope of Pluronic F127 in the following.

Following the description of the chitosan copolymer in terms of availability and generation, the copolymer types are explored in this section. The types of copolymers refer to the structure being ABA (triblock) or any other structure type. Hence, the interest in copolymers is raised referring to the ability of sol-gel transition as described in section 2.2 of the literature. The Pluronic copolymer F127 is referred to as an ABA structure triblock copolymer having the form of PEO-PPO-PEO. Figure 2.7 illustrates the Pluronic of the structure ABA being triblock.

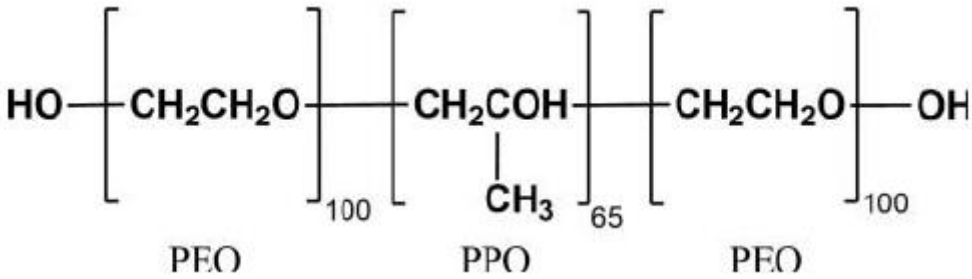

Figure 2.7: Triblock copolymer of PEO-PPO-PEO structure (Akash, et al., 2015).

These copolymers are temperature sensitive hydrogels are described in section 2.2 of the literature. In addition, they are usually referred to as Pluronic copolymers (Gutierrez, et al., 2017). These copolymers exist at low temperatures in their liquid state in order to be injectable. Another study assessed the Pluronic F127 in its liquid state, where the heating applied on the copolymer was attempted from 4℃ towards the human average body temperature. Such copolymer was used in drug delivery systems or vehicles in order to be a therapeutic agent in biomedical applications. Most studies on Pluronic F127 focuses on the controllability in injection, where it was discussed that the chemical bonding or chains is mainly applied through the incorporation of thiol (Liu, et al., 2015). It should be noted that the formation of these copolymers could be categorized as block copolymers which vary upon the structure (Niu, et al., 2011). In the same study, the triblock copolymer was assessed in terms of

its block length as it affects the applicability in drug delivery systems, where they denoted the calculation following the ratio of PEO to PPO chains. The presentation of the triblock copolymer in Figure 2.7 have several requirements in terms of its usage in drug delivery system. Hence, several studies assessed their applicability in drug delivery systems and complex applications in therapeutic approaches.

2.5 RHEOLOGY

In drug delivery systems, polymers are being used as mentioned in the previous sections of the literature, where hydrogels-based polymers chain are being used. Hence, these polymers are studied referring to the manipulation to deliver optimised behaviour in terms of flowing in the delivery systems. Therefore, understanding the rheology of these hydrogels should be researched. In the following section, rheology is described in order to give an intel towards the manipulation of the data at later stages of the project.

2.5.1 Flow behaviour

The rheology is understood as the variation of the polymeric flow within a delivery system. Hence, the interaction between the flow layers have to be assessed. It was mentioned in the shear stress sensitive polymer section of the literature that the polymers will undergo shear thinning and thickening, which elaborates on the rheological parameters, such as, the viscosity and shear rates occurring between the polymer and the delivery system (Mezger, 2014). It was denoted in the Mezger notebook that the molecular mass of the polymers in the study alters based on the shear variation as illustrated in Figure 2.8.

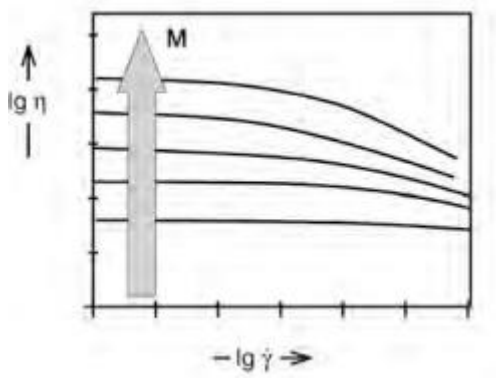

Figure 2.8: Variation of molecular mass at zero-viscosity shear application (Mezger, 2014).

The flow of the polymers in the intended delivery systems experiences stresses that are denoted by the shear rate occurring at their layers. Eq 2.1 illustrates the viscosity dependence of the addressed fluid.

$$\eta = \frac{\tau}{\dot{\gamma}} \; Eq\ 2.1$$

In order to assess the viscosity occurrence during the flow application, Figure 2.7 illustrates a schematic of two plates to illustrate the velocity distribution.

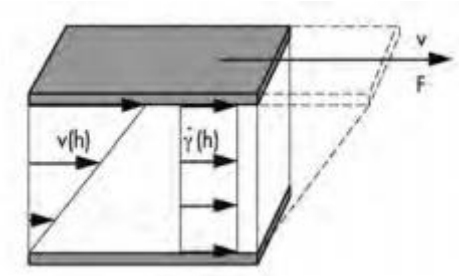

Figure 2.9: Two moving plates with shear created on the flow layers.

The calculation of the shear occurring on the polymer or the fluid taking place between the plats, Eq 2.2 takes place in this section.

$$\dot{\gamma} = \frac{v}{h} \; Eq\ 2.2$$

It was discussed in the literature that shear stress sensitive polymers undergo shear thinning and shear thickening, which is a rheological aspect illustrates in Figure 2.10 for more understanding in terms of the liquid behaviour.

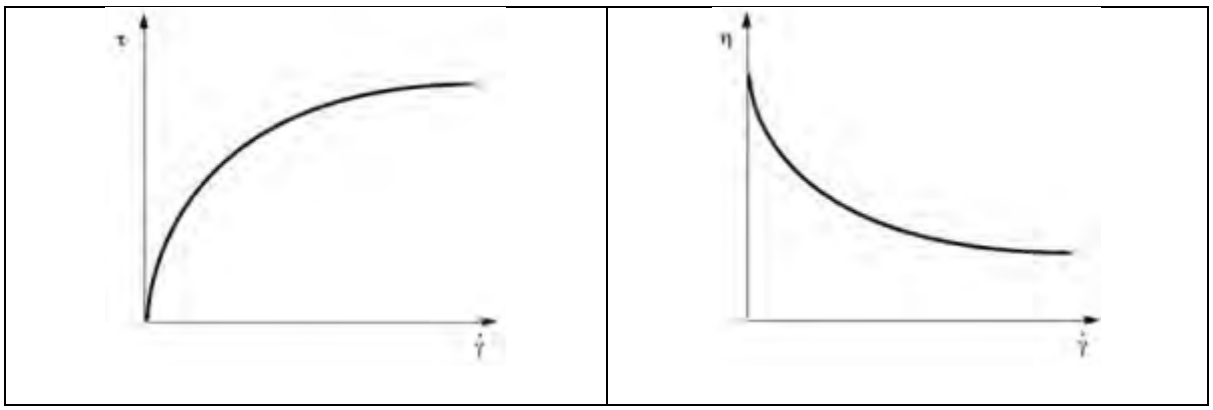

Figure 2.10: Shear thinning and shear thickening of polymers flow (Mezger, 2014).

The behaviour described from Mezger handbook refers to the behaviour of Newtonian fluids, where the stress and the strain ocuring at the interaction layer between the polymer and the delivery system should be linear. This information helps in addressing the type of flow simulation study in polymers based on the rheological assessment. Another critical factor to be assessed when talking about rheology was reported to be the temperature, where several studies referred to the temperature sensitive polymers and their sol-gel transition. Referring the shear occurrence at the polymer levels, the temperature could be a dependent factor in the transition as illustrated in Figure 2.11 on the shear thickening.

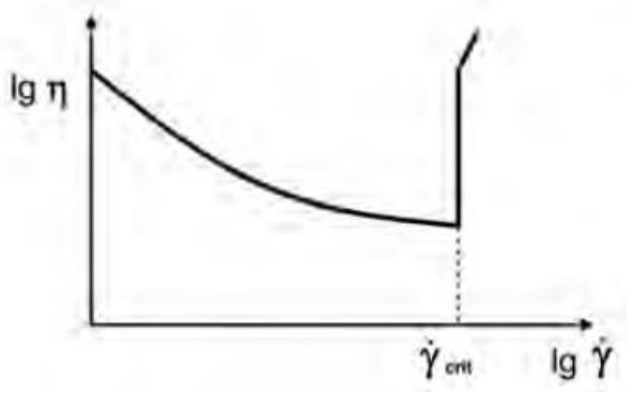

Figure 2.11: Viscosity of an elastomer reaching the critical shear rate (Mezger, 2014).

It is noted that the reaching of the critical shear rate increases dramatically the viscosity of the studies polymer. The temperature assessment in this aspect refers to the high or low temperature to attain the crystallisation of the polymer, where upon this phenomenon, the viscosity has to increase dramatically as illustrated in Figure 2.11. The testing of such behaviour refers to the capillary rheometer usage described in the following section.

2.5.2 Capillary rheometer

Capillary rheometer is the test rig to test the flow behaviour and monitor the viscosity variation of tested elastomers or polymers. The capillary Rheometry was defined in (Mezger, 2014) based on the usage of an electric drive to drive a piston at a speed range between 0.02µm/s to 40mm/s depending on the intended application. Figure 2.12 illustrates a schematic of the capillary rheometer for further understanding.

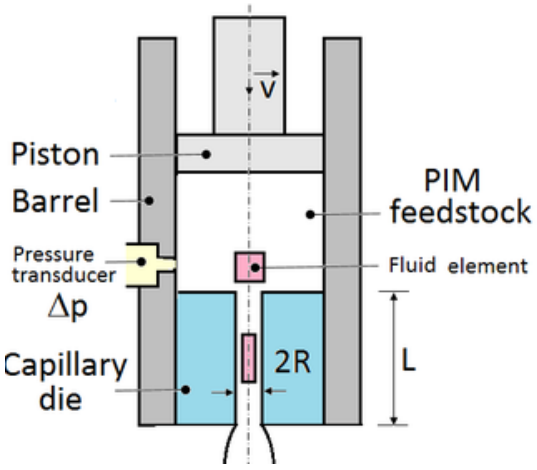

Figure 2.12: Schematic of capillary rheometer used in (Hnatkova, et al., 2016).

Mezger reported the corrections for the data used in flow analysis based on the viscosity variation and shear rate. The corrections were generated by Rabinowitsch and Bagley in (Bagley, 1957). These corrections of the data are applied in terms of the flow behaviour analysis of polymer melts. The usage of the Hagen/Poiseuille relation without the corrections may lead to errors in the measurements. The error could reach

high values of more than 20%. Therefore the corrections according to Bagley and Weissenberg/Rabinowitsch should be applied. Referring to the Hagen/Pouseuille equation to calculate the shear rate on the walls is presented in Eq 2.3.

$$\dot{\gamma} = \frac{4\dot{V}}{\pi R^3} \quad Eq\ 2.3$$

With the dimensions of the cylinder used to press the polymeric melt, Eq 2.3 is presented in Eq 2.4.

$$\dot{\gamma} = \frac{4\pi R_1^2 v}{\pi R_2^3} \quad Eq\ 2.4$$

2.6 SUMMARY

After the research conducted on the hydrogels' specifications, types, and application, the challenges are presented as a summary for the literature review section. The stimulation of the hydrogels is one of the main faced challenges based on their sensitivity as described in section 2.2 of the literature. The hydrogels are becoming a centre of interest in drug delivery as therapeutic applications in medical and healthcare fields. This is referred to their ability in being controlled and non-invasive. All the applications to date of these hydrogels in cancer therapy or drug dosage application is still being studied in clinics, where the actual applications are still being tested based on their sensitivity to external factors. Mainly, the faced challenges of these hydrogels are emphasised on their applicability in human bodies without addressing any toxicity measures. In addition, their repetitive manufacturing upon high demand should be understood. However, in this literature it was seen that the most studied hydrogel in terms of the shear stress sensitive types is the tri-block copolymers based on several forms, such as, F127, F108, L61, etc. Hence, the assessment of the viscoelastic

behaviour of these polymers in drug delivery systems have potential benefits in terms of the biomedical and healthcare application advancements.

3 METHODOLOGY

3.1 INTRODUCTION

In this chapter of the project, the methodology and the steps required to generate the design of the instrumented syringe for the drug delivery system is assessed. In addition, this chapter comprises the steps taken for the data collection in order to assess the dynamical behaviour of the fluid used as the triblock hydrogel used in the experiment.

3.2 DESIGN OF THE INSTRUMENTED SYRINGE

In drug delivery systems, instruments are used such as the syringe which should be designed in an optimal approach. The optimal approach for the syringe design relies on several factors, such as, the pressure occurring at the syringe walls, the dimensions of the syringe, the viscosity, and the shear rates. Therefore, the computation of the pressure should be assessed for better design generation. Figure 3.1 illustrates the main parts of the syringe.

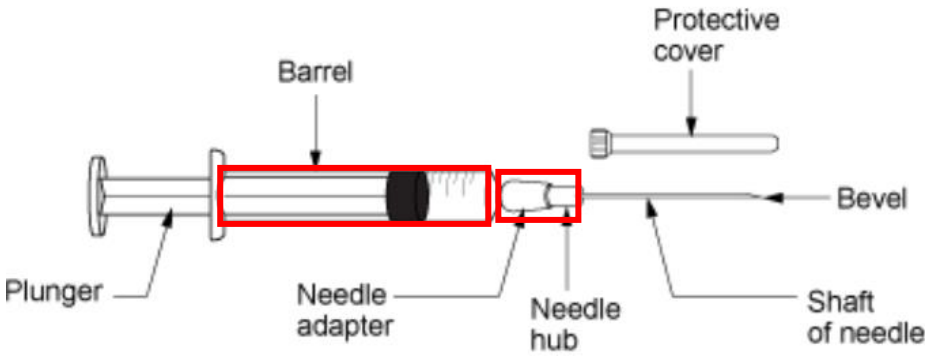

Figure 3.1: Syringe schematic with markings on the critical parts.

It could be noted from Figure 3.1 that the critical parts to be designed for the injection are highlighted in Red. The pressure differentiation between the parts of the syringe are governed by Hagen-Poiseuille equation illustrated in Eq 3.1.

$$\Delta P = \frac{8\eta LQ}{\pi R^4} \quad Eq\ 3.1$$

Throughout the pushing mechanism of the syringe, a friction force will be created on the inner walls of the syringe. This is related to the visco-elastic effect of the tri-block copolymer used in the process. Hence, this would result in a shear rate calculated as illustrated in Eq 3.2.

$$\dot{\gamma} = \frac{4Q}{\pi R^3} \quad Eq\ 3.2$$

Eq 3.1 is used for the design of the syringe following the optimisation of the required dimensions set for the analysis at later stages of the report. In addition, the shear rate equation illustrated in Eq 3.2 is used for the dynamical behavioural analysis of the fluid throughout the pushing process. It was mentioned earlier that a pressure difference will occur between the needle hub and the barrel, where this pressure difference is illustrated in two equations Eq 3.3 and Eq 3.4.

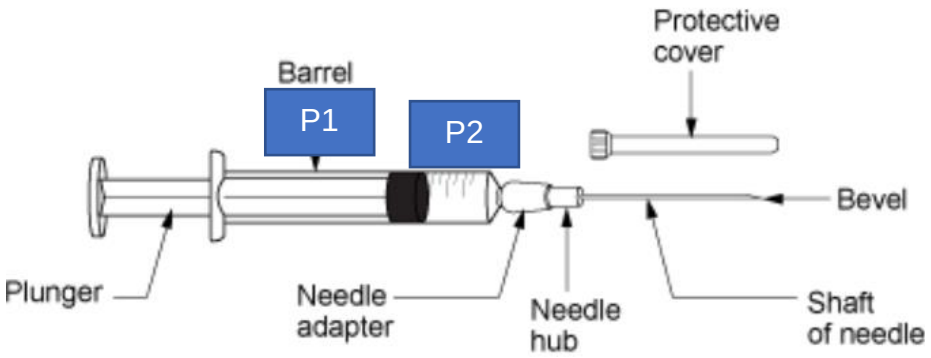

Figure 3.2: Syringe schematic with showing the pressure difference between the barrel and the needle.

$$\Delta P_{syringe} = \frac{128\eta L_1 Q_1}{\pi d_1^4} \quad Eq\ 3.3$$

$$\Delta P_{Needle} = \frac{128\eta L_2 Q_2}{\pi d_2^4} \quad Eq\ 3.4$$

Following the calculations of the difference in pressure drop at the syringe level, the viscosity occurring at different pressures should be obtained from the laboratory analysis of the copolymer behaviour (Rheometry analysis). It should be noted that the temperature range should be starting at room temperature (20℃) and finalised at the body temperature (37℃). The body temperature is selected as the final temperature because the polymeric hydrogel is intended to be injected in the human body. It is noticed that Eq 3.3 and Eq 3.4 mentioned the length and the diameter of the intended syringe, where Figure 3.3. illustrates the dimensions required to be optimised for the barrel and the needle hub.

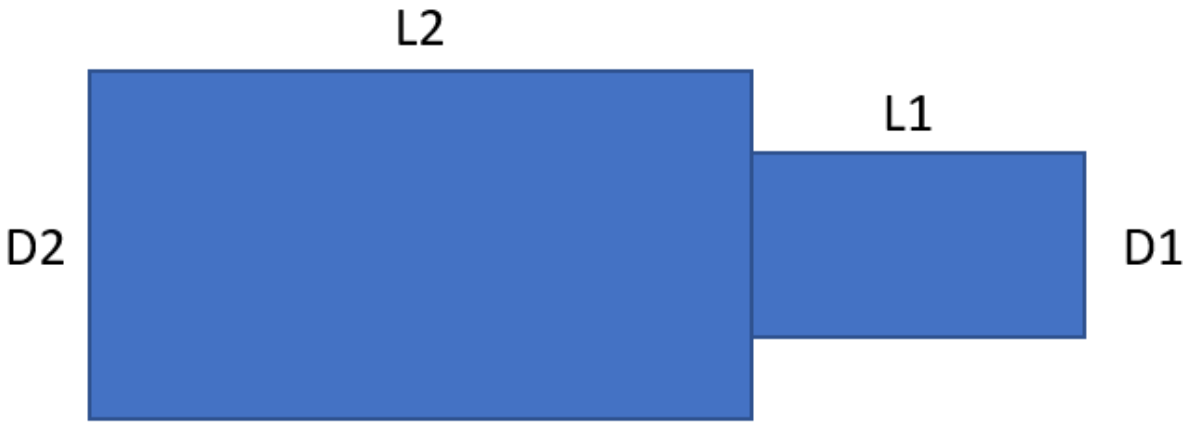

Figure 3.3: Dimensions of the intended syringe.

3.3 DYNAMICAL BEHAVIOUR OF THE TRI-BLOCK COPOLYMER

In this section of the methodology, the dynamical behaviour steps of the fluid in the syringe will be investigated. A similar investigation took place in (Agudo, et al., 2012), where they investigated the flow of the fluid in the syringe with the resultant illustrated in Figure 3.4.

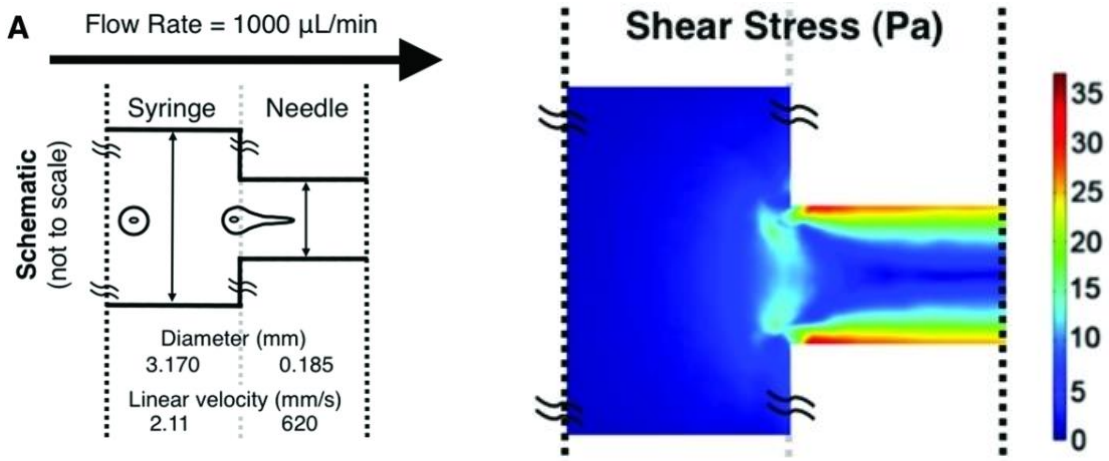

Figure 3.4: illustration of the syringe design with the dynamical behaviour analysis of the fluid (Agudo, et al., 2012).

From the study, they concluded the loss and storage modulus occurring at the syringe walls. All the analysis referred to the shear rate, temperature, and viscosity occurring on the fluid level which is similar to the approach to be undertaken in this study. In order to assess the fluid behaviour in the syringe barrel and needle hub, SolidWorks software flow simulation should be used to model the flow and visualize the stress occurring at the walls level.

3.3.1 Syringe design

The design of the syringe illustrates a critical aspect of the study, where it varies the behaviour of the Pluronic polymer to be used in the injection exercise. SolidWorks software is used for the design of the syringe. In terms of the dimensions of the syringe, the ratio of the syringe to the needle was taken at 17 in (Agudo, et al., 2012). This ratio is considered in this study. Therefore, the dimensions assumption are taken as follows:

1) Syringe diameter: 35mm.
2) Needle diameter: $\frac{35}{17} = 2mm.$
3) Needle length: 40mm.
4) Syringe length: 30mm.

The dimensions considered for the needle and the syringe allow us to design the intended object on SolidWorks with the given dimensions. In addition, there are other assumptions to be taken in reference to the flow of the Pluronic F127 in the syringe and the needle and they are mentioned in the following:

1) Flow rate: 10000µL/min.
2) Flow: Laminar.

3.4 VISCOELASTIC ANALYSIS OF PLURONIC F127

The next stage of the analysis refers to the viscoelastic analysis of the Pluronic F127, where the analysis refers to the monitoring of the viscosity against temperature and shear rate variation. In order to generate such results, a rheometer is used as an instrument to study the viscoelastic properties of the Pluronic F127. The Pluronic F127 is studied at a temperature range between 5℃ and 40℃, where this allows the monitoring of the Pluronic F127 behaviour based on the temperature variation. Also, it was mentioned in the literature review that these polymers undergo a variation in the molecular weight, which illustrates an effect on their behaviour. Therefore, three different concentrations were considered in the analysis:

1) 15%.
2) 20%.
3) 25%.

The different concentrations are considered as different samples that undergo the same testing in the rheometer to monitor the viscosity at different shear rates and temperatures.

4 RESULTS

In this result section, the steps mentioned in the methodology chapter are executed. The first step is the study the viscoelastic analysis from the data given from the Rheometry analysis. The next stage is to generate the required calculations for the syringe design to withdraw the pressure drops occurring in the syringe. The next stage is to design and simulate the Pluronic F127 as an injectable polymer in the syringe. The third and final stage is the simulation of the flow withing the syringe to compare the behaviour of the F127 Pluronic in the syringe and the needed during injection.

4.1 VISCOELASTIC ANALYSIS OF THE LABORATORY DATA

In this section of the results, the collected data from the laboratory for the Pluronic F127 based on the rheological analysis between a temperature of 5 and 40℃ at different shear rates is presented and discussed. In addition, a follow-up analysis is applied on the data to contrast the main difference of concentration variation and shear rates effect.

4.1.1 Viscosity at different concentrations

The first analytical data is visualized in Figure 4.1 showing the viscosity variation of the F127 at different concentrations.

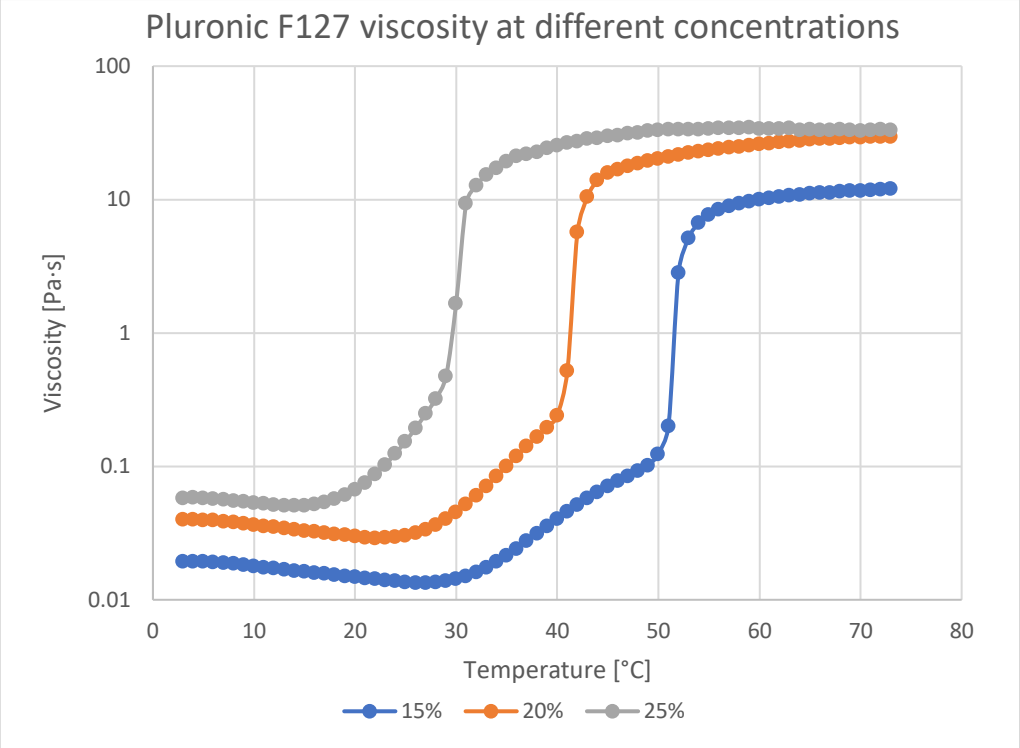

Figure 4.1: F127 viscosity analysis at different concentrations.

It should be noted that the viscosity is varying at the similar shear rate set at 10 s^{-1}. It is noted from the plot that the increase in temperature have a direct impact on the viscosity increase. Also, the increase in concentration of the F127 Pluronic increases the viscosity at noted in Figure 4.1. However, the rate of viscosity increases between the concentration of 15% to 20% is higher than the rate of increase between the concentration 20% to 25%. It should be noted that this is not an accurate comparison since the logarithmic scale was taken on the viscosity axis. It is also noticed from the plot that the leap increase in viscosity is occurring at different temperatures, where for the concentration at 15%, the leap occurs at approximately 50℃. For the 20% concentration, the leap occurs at approximately 39℃. However, for the highest concentration, the temperature leap occurs at a low temperature of 30℃. This reveals that the increase in concentration decrease the sol-gel transition temperature of the Pluronic F127. Following the plot generated in Figure 4.1, the data given from the

laboratory is applied at four different shear rates, of 10^{-1}, 20^{-1}, 50^{-1}, and 100^{-1}. The same plots were generated for the different shear rates as illustrated in Figure 4.2.

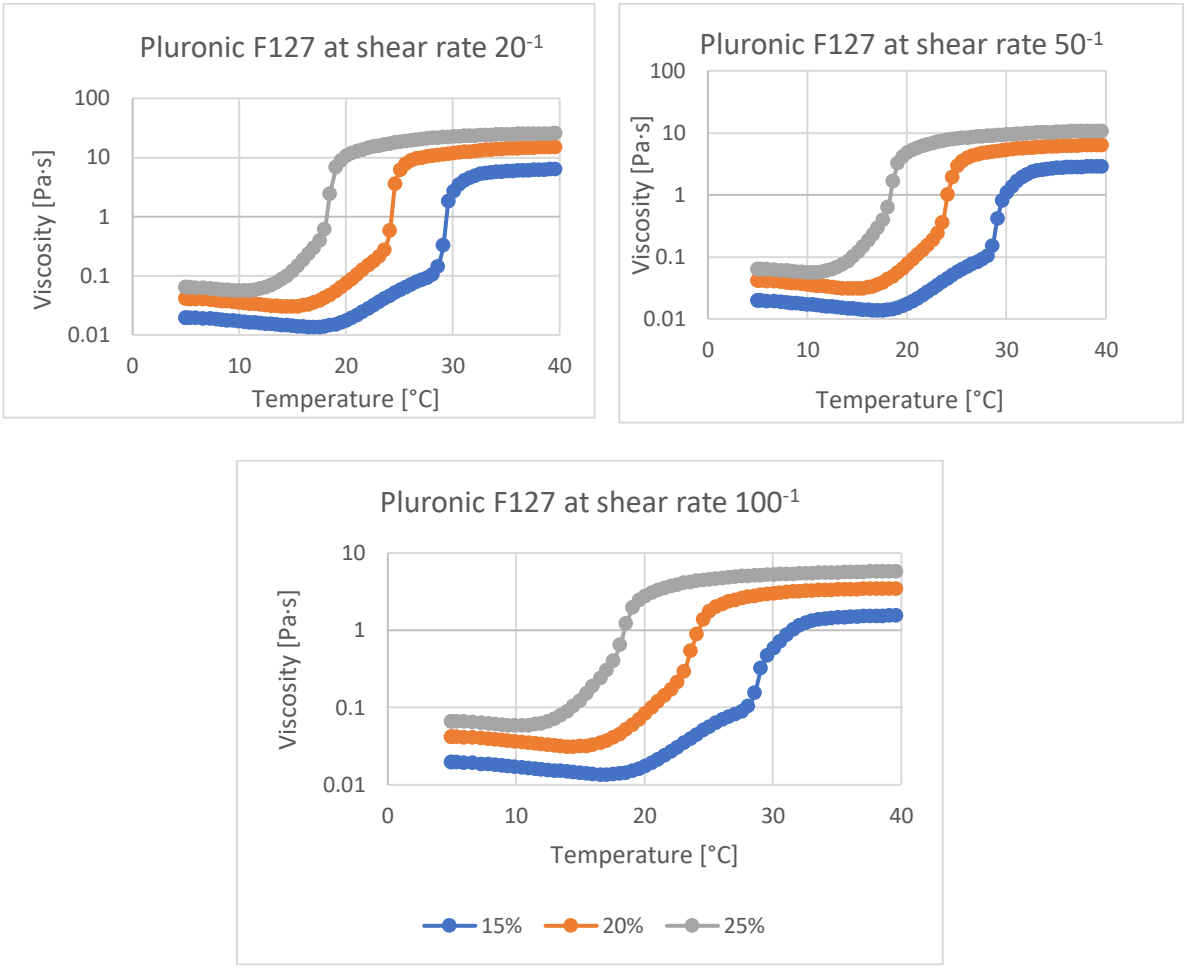

Figure 4.2: Viscosity of Pluronic F127 at different shear rates and concentration.

The same analysis applied on Figure 4.1 implies on Figure 4.2, where there difference between the logarithmic scale values is not obvious; therefore, the plots have to be generated based on the fixation of the concentration and varying the shear rate. Figure 4.3 illustrates the variation of the viscosity at different shear rates with fixing the concentration at 15%.

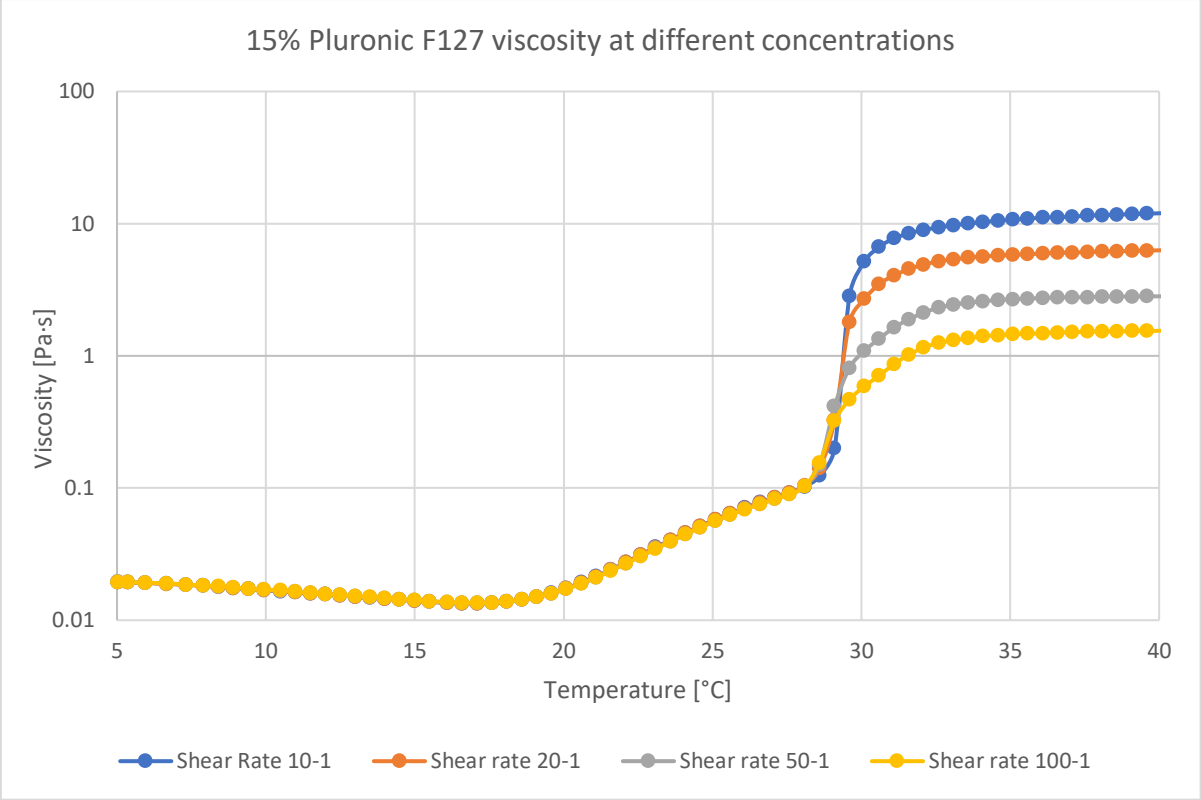

Figure 4.3: Viscosity of F127 Pluronic with varying the shear rate.

Following the curve behaviours in Figure 4.3, the shear rate decreases with the increase in viscosity. This means that the viscosity increase affect the shear stresses created on the wall of the polymers in a decrement way. This is logical in terms of the surface contact created on the walls of the polymer in relation with the shear rate. Another aspect noted in this plot is the temperature effect, as it varies from the analysis applied on the previous section at different concentrations. The viscosity leap occurring at the same temperature. This validates the true plots applied in the previous section, where the Pluronic used in Figure 4.3 has the same concentration. This validates the discussed information in terms of the temperature variation based on the concentration.

Following the analysis applied on Figure 4.1 and Figure 4.3 shows that the concentration and the shear rates have direct effect on the viscosity of the Pluronic F127 as described in the aforementioned analysis.

4.1.2 Follow-up analysis

In this section, a follow up analysis is applied to check the viscosity variation referring to different shear rates. This will allow a building relationship between the shear rates and the leap in the viscosity variation. In order to apply this analysis, a single concentration should be taken into consideration. Also, this analysis helps in showing visually in an easy way how the viscosity is affected by the shear rate. Figure 4.4 illustrates the viscosities at the end point of the analysis.

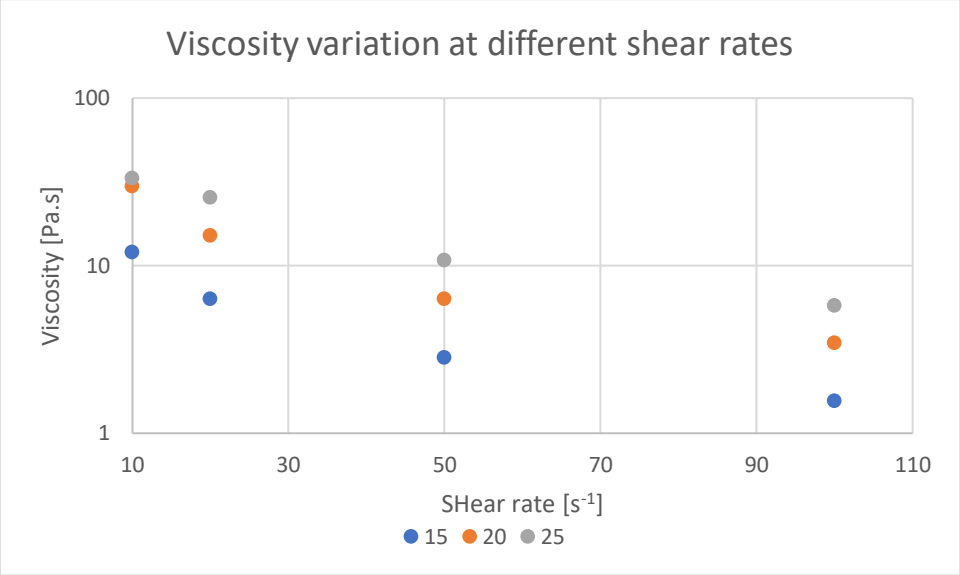

Figure 4.4: Variation of the viscosity based on the shear rate.

Figure 4.4 shows the different concentrations of the Pluronic F127 used in the laboratory along with different shear rates. It should be noted that the data taken in Figure 4.4 is based on the temperature of 40.1℃. This temperature is the end point of the temperature monitoring. It is noted that the increase in the shear rates clearly decreases the viscosity as they are inversely related. Also, the concentrations increase clearly increases the viscosity of the material in terms of being more gel than solution.

4.2 PRESSURE CALCULATION FOR THE SYRINGE

In this section, the pressure drop that will occur in the syringe is calculated based on the assumptions considered in the methodology chapter of the project. The pressure calculation follows Eq 3.1. In order to generate the required calculations for the pressure drop, the total pressure should be calculated by the addition of both sides of Eq 3.1 that results in the following.

$$\Delta P_{Total} = \Delta P_{Syringe} + \Delta P_{Needle}$$

$$\Delta P_{Total} = \frac{128\eta L_1 Q_1}{\pi d_1^4} + \frac{128\eta L_2 Q_2}{\pi d_2^4}$$

Q illustrates the injection rate of the needle, which is taken the same in the needle and in the syringe. Therefore, the total pressure is calculated following Eq 4.1.

$$\Delta P_{Total} = 128\eta Q \times \left(\frac{L_1}{\pi d_1^2} + \frac{L_2}{\pi d_2^2} \right) \; Eq\ 4{,}1$$

The pressure drop could be calculated for the all the concentrations given of the Pluronic F127 based on its viscosity at room temperature. The room temperature is assumed to be 20℃. Therefore, the data is taken from the temperatures of 20℃. An example is applied for the calculations in the following:

$$\Delta P_{Total@15\%} = 128\eta Q \times \left(\frac{L_1}{\pi d_1^2} + \frac{L_2}{\pi d_2^2} \right)$$

$$\Delta P_{Total@15\%} = 128(0.0175)10 \times \left(\frac{0.03}{\pi 0.35^2} + \frac{0.04}{\pi(2 \times 10^{-3})^2} \right)$$

$$\Delta P_{Total@15\%} = 22.4 \times (0.078 + 3183.09) = 3184.83$$

Following the calculations for all the pressures at the different viscosity, Figure 4.5 is plotted to show the pressure variation based on shear rate change.

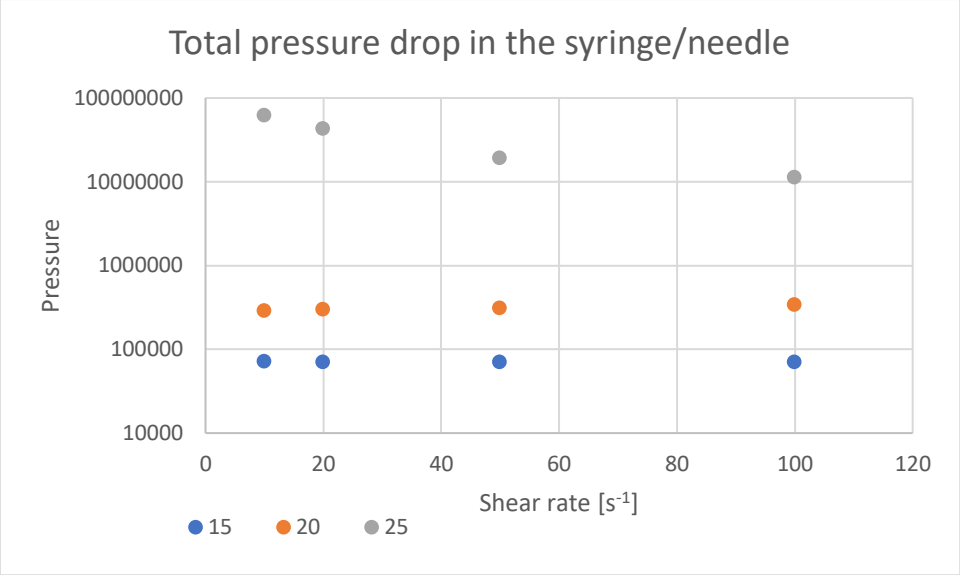

Figure 4.5: Total pressure variation in the syringe based on the concentration change of the F127 Pluronic.

It is noted that the pressure drop decreases with the decrease in the concentration of the Pluronic. In addition, the increase in the shear rate have small effect on the total pressure drop based on the concentrations of 15% and 20%. However, for the concentration of 25%, the viscosity varies at the room temperature at different shear rates; therefore, the pressure drop decreases with the increase in the shear rates.

4.3 Design of the Syringe/needle

In this section, the design of the syringe/needle to be used for the drug injectability is designed on SolidWorks in order to apply flow simulation of the Pluronic F127 on Simulation Flow on SolidWorks. Figure 4.6 illustrates the design of the syringe/needle following the assumed dimensions.

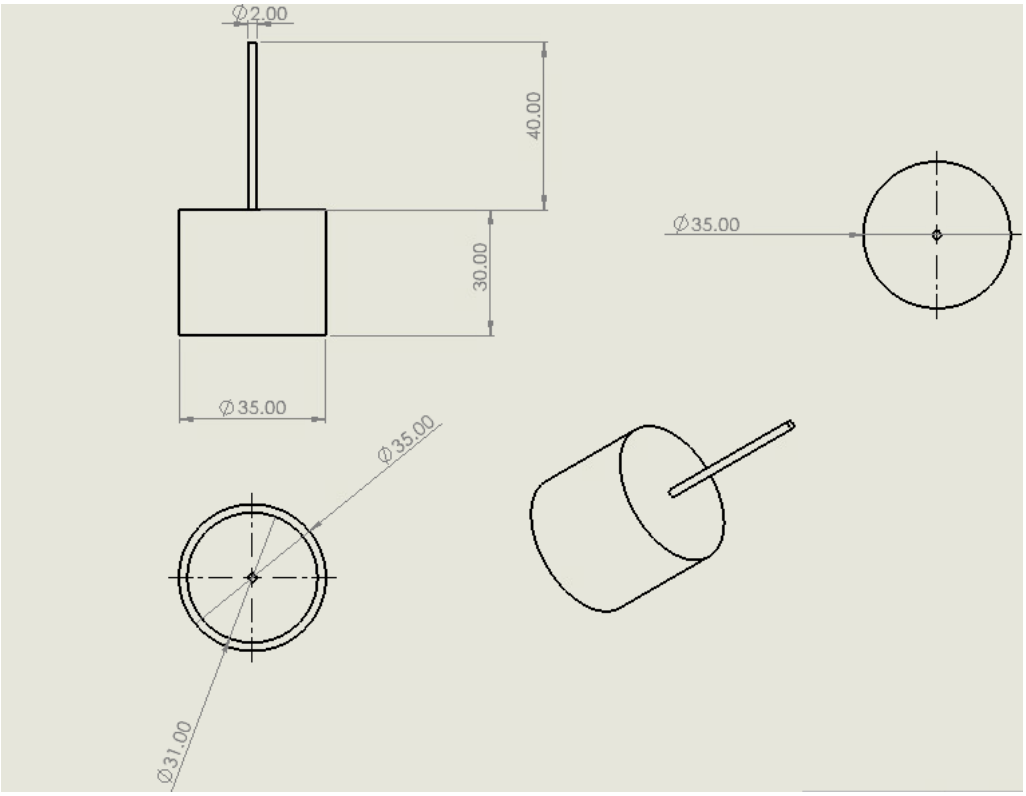

Figure 4.6: 2D schematic of the designed syringe needle device.

The design illustrated in Figure 4.6 was the 2D schematic with the considered dimensions of the syringe needle. Figure 4.7 illustrates the 3D design of the needle with the filleted shapes.

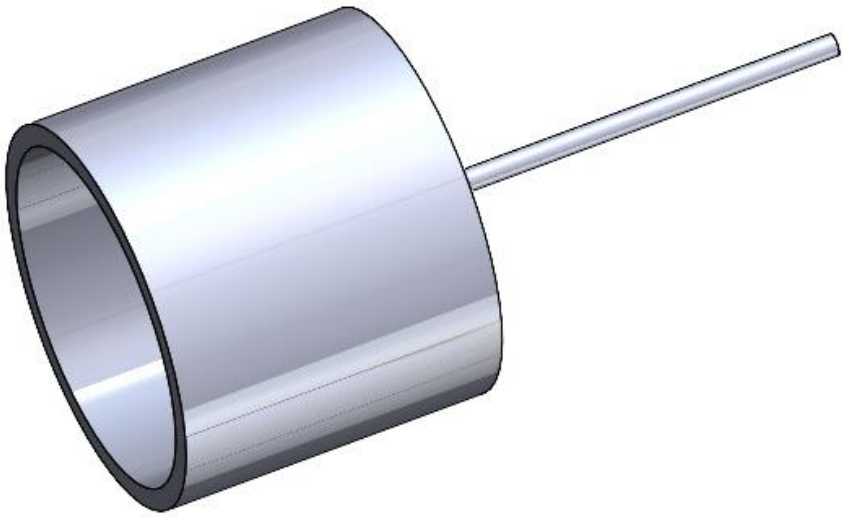

Figure 4.7: 3D view of the designed needle.

4.4 SIMULATION FLOW OF THE PLURONIC F127

In this section of the results, the simulation of the Pluronic laminar flow inside the syringe is applied using the simulation flow tool on SolidWorks software. The required steps and assumptions inserted in the simulation setting are defined and justified in the following.

4.4.1 Building the simulation

An internal flow simulation is selected in SI units with selecting the analysis type as gravity as illustrated in Figure 4.7.

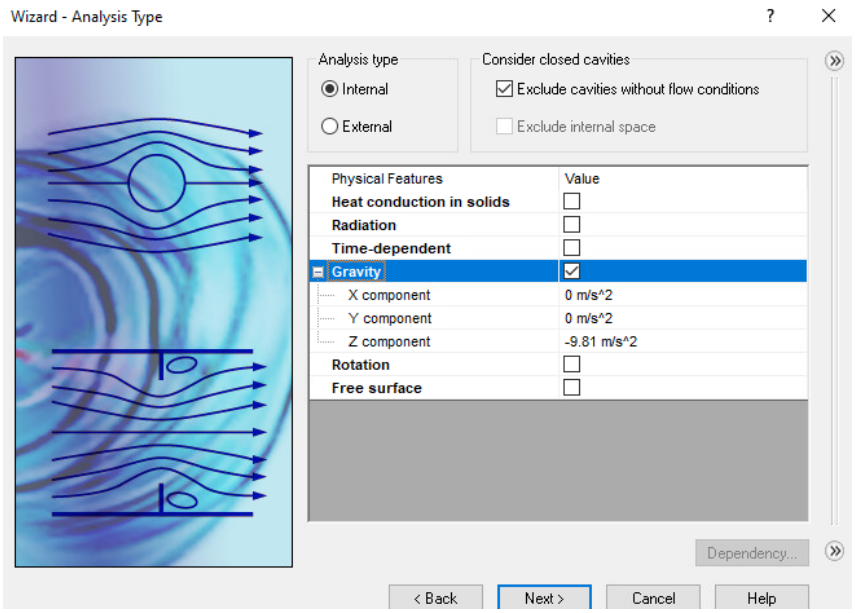

Figure 4.8: Gravity based analysis for internal flow inside the syringe.

The next step is to apply the required properties of the pluronic fluid used in the study; however, Pluronic F127 is not defined in SolidWorks, which means it has to be user defined. Then no heat transfer in the walls is applied which means an diabatic process is considered. Room temperature is considered at 20℃. Also, the flow speed has to be defined in the initial conditions as it was taken at 2.11mm/s similar to the study by (Agudo, et al., 2012). In order to generate the enclosed volume of the simulation, lids have to inserted as illustrated in Figure 4.9.

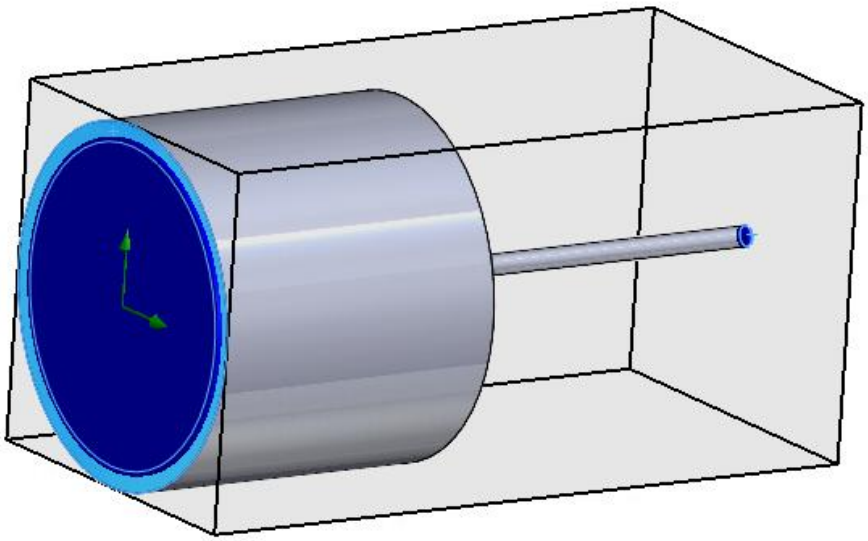

Figure 4.9: Creating lids within the openings of the syringe.

The next stage is to select the internal face of the lid to initiate the boundary conditions, where the flow rate is taken at 10000µL/min. In SI units:

$$10000\mu\frac{\mathrm{L}}{\mathrm{min}} = \frac{10000 \times 10^{-6} L}{60s} = 1.667 \times 10^{-4} L/s$$

4.4.2 Results from the simulation

Following a standard mesh in the simulation with the required flow rate set inside the syringe, the simulation is ran with the results generated. First, the simulation is checked in the list of goals set as illustrated in Figure 4.10.

List of Goals

Name	Current Value	Progress	Criterion	Averaged Value
GG Average Dynamic Viscosity 1	0.00100051 Pa*s	Achieved (IT = 40)	1.00051e-11 Pa*s	0.00100051 Pa*s
GG Average Shear Stress (Y) 2	0.0142795 Pa	Achieved (IT = 52)	0.000550473 Pa	0.0138209 Pa

Figure 4.10: Goals set prior to the simulation with successful output.

The value of the average shear stress occurred in the Y direction, which means the direction of the flow was averaged at 0.01382Pa. Also, the pressure generated in the simulation refers to the contour plot shown in Figure 4.11.

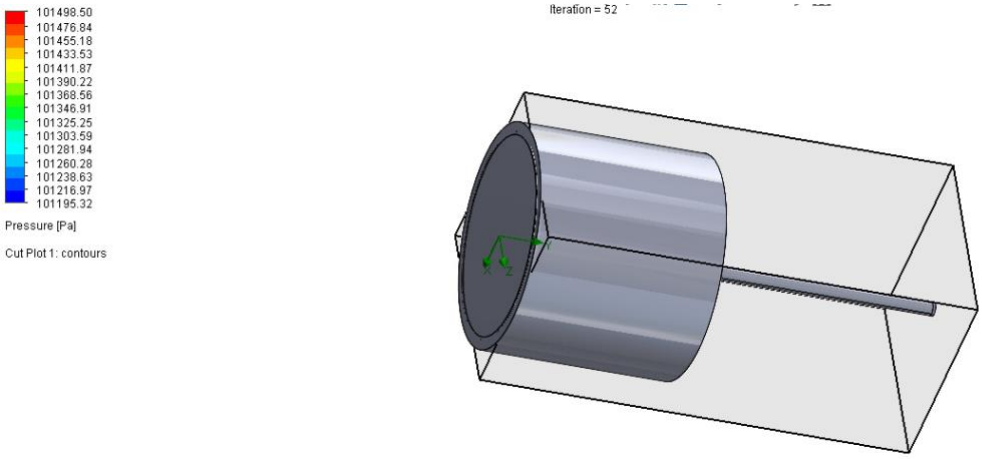

Figure 4.11: Contour plot of the pressure occurred with the syringe and needle.

The maximum pressure occurred in the syringe was at 101498.5 Pa. Based on the input parameters considered for the Pluronic F127 in Abacus, the pressure was calculated referring to Figure 4.5 to be 71303Pa. Hence, there is a big difference in terms of the calculated and the simulated data with the percentage error calculated as follows:

$$\%Error = \frac{101498.5 - 71303}{101498.5} = 29.7\%$$

This simulation and the calculation made earlier were referring to the Poiseuille equation, which was discussed in (Mezger, 2014) to have higher than 20% error in rheological assessment. Hence, a cut plot is shown in terms of how the Pluronic F127 is reaching the end point of the needle flowing from the syringe.

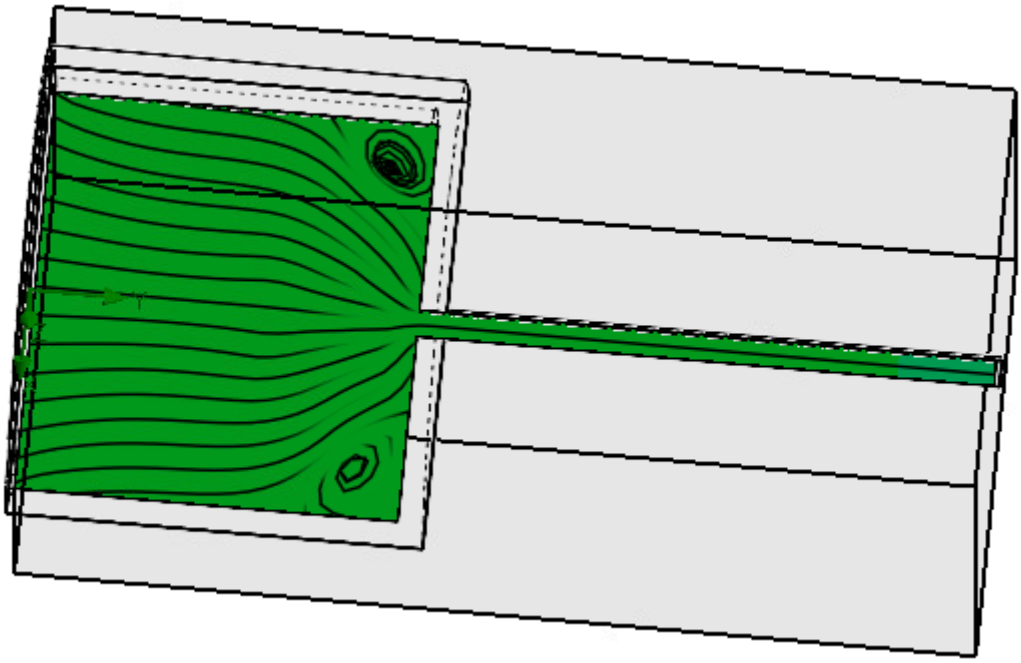

Figure 4.12: Flow of the Pluronic F127 in the syringe to the needle flow.

Following the simulation addressed in this section, the generated results from the laboratory could be inserted in the user defined Pluronic F127 properties in order to compare all the data generated in the analysis along with the data assessed on the laboratory based on the Rheometry usage.

5 DISCUSSION

In this chapter of the project, the results generated in the fourth chapter are discussed in the light of the Pluronic F127 success in being used in drug delivery systems along with the comparison between the different concentrations to assess the optimum one. Hence, the simulation results are assessed and discussed in this section based on the output generated in terms of the pressure occurring in the syringe and the needle upon the injection of the Pluronic F127. The discussion comprises three different parts, where the first one focuses on the conctration and shear rates effect on the viscosity of the fluid. The second part discusses the pressure difference within the syringe and how they affect the behaviour. Finally, the simulation is assessed based on the results generated and the limitations faced.

5.1 CONCENTRATION AND SHEAR RATES

In this section the concentration and shear rates are discussed in terms of their effect on the viscoelastic properties of the Pluronic F127. It should be noted that there are three different concentrations at 15%, 20%, and 25% and four different shear rates as follows, $10s^{-1}$, $20s^{-1}$, $50s^{-1}$, and $100s^{-1}$. The testing of the Pluronic F127 was conducted at a temperature range between 5℃ and 40.1℃. The testing range of the Pluronic F127 is monitored to check the variation in the viscoelastic properties at different temperatures. Figure 4.1 showed that the increase in concentration has a direct impact on the viscosity increase, where this is attributed to the sol-gel transition of the Pluronic F127 as it is more viscous when the molecular weight in the mixture with water increase as reported in (Shriky, et al., 2020). Figure 5.1 illustrates the results with similar concentration of the Pluronic F127.

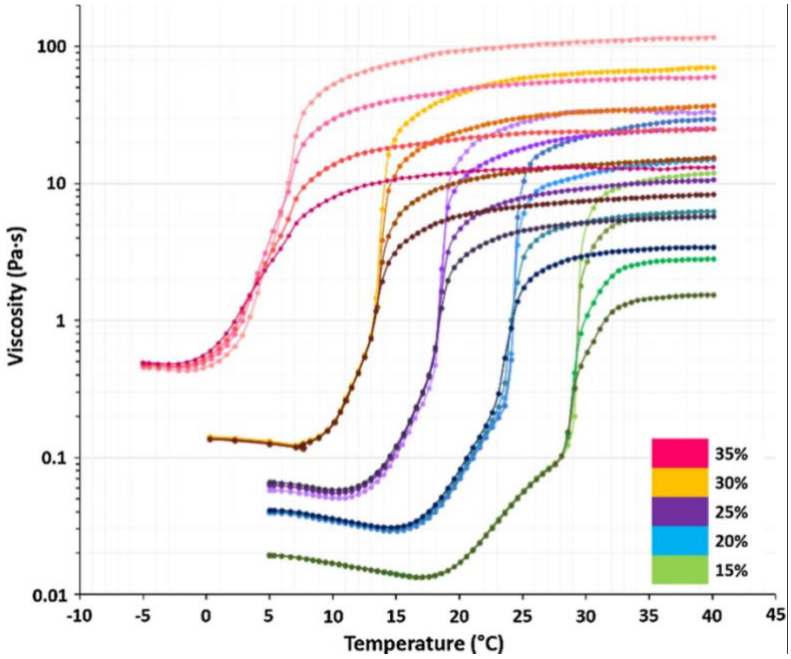

Figure 5.1: Behaviour of the Pluronic F127 viscosity at different concentrations (Shriky, et al., 2020).

It should be noted that the temperature range differed in the study; however, viable discussion could take place on the increase in viscosity with the increase of the concentration. Another study by (Khateb, et al., 2016) reported the gelation temperature of the Pluronic F127, where it was revealed that the gelation temperature varies between 28 and 74℃. However, the gelation temperature of the product was assessed with mixing it with F68 Pluronic. This alters the values of the gelation temperature. However, in their studies assessed the gelation temperature of the concentration of 0:20% F68/F127, which means pure Pluronic F127 and the gelation temperature was 28.1℃. Comparing this value with Figure 4.1 at 25% concentration shows that the temperature in our study showed a sol-gel transition temperature of 29℃. In terms of the monitoring of the viscosity at different shear rates, it was noted from Figure 4.3 that the shear rate increasing causes the decrease in viscosity of the Pluronic F127. This is attributed to the friction force on the membrane of the Pluronic F127. According to (Wei, et al., 2002) the viscous modulus is the resultant of this effect as it has the same curve behaviour as the viscosity. Also, Figure 4.4 illustrated the

viscosity decrease at different shear rates. In addition, Figure 4.4 summarised the behaviour of the Pluronic F127 based on the concentration and shear rates. The rate of viscosity changes between the concentrations and the shear rates values is proportional to the rate of increase. It should be noted that the comparison was taken at the last point of the viscosity plots, which means at 40℃, which is the highest gelation point of the material.

5.2 PRESSURE DROP

The pressure drop refers to the injectability of the Pluronic F127 in a syringe, where in the methodology and results section of the project, a syringe/needle was designed for such purpose. Prior to the design and analysis of the syringe, the pressure drop is calculated based on the assumptions taken for the syringe dimensions. Also, the pressure drop was calculated at all the different concentrations and shear rates. However, it should be noted that the calculations were undertaken based on the room temperature at 20℃. This is an essential aspect of the calculation as reported in (Agudo, et al., 2012), where the injection should start at room temperature. Referring to Figure 4.5, the pressure drop show that no big differences are denoted based on the variation in the shear rate at specific concentration. However, the difference in concetration altered the pressure drop results. Hence, the increase in concetration caused the pressure drop to increase relatively with the viscosity. The reason behind the similar pressure drop between the different shear rates refers to these values cancelling each other or overcoming each other in an injection exercise of the polymer. It is noted that the increase of the concentration towards 25% allowed the variation of the pressure drop between the syringe and the needle at higher shear rates at $100s^{-1}$

5.3 SIMULATION OF THE FLOW

The design of the syringe and its analysis were mainly refeering to the study applied by (Agudo, et al., 2012), where the assumptions were taken based on the flow rate, and the ratio of the dimensions for the needle. However, the dimensions themselves were not similar. Regarding the input of the simulation, the Pluronic F127 was created based on a compressible fluid with a density similar to water at 998kg/m^3. The results generated from the simulation mainly referred to the pressure occurring at the liquid level, where a 29.7% error was revealed between the calculated and the simulated pressure drop. It should be noted that the simulation considered the concentration of the Pluronic F127 at 15% along with a shear rate of 10s^{-1}. It should be noted as well that these values could not be inserted in SolidWorks simulation flow, however, these values are illustrated in the selection of a temperature of 293K (20℃) and a dynamic viscosity of 12Pa.s (refer to Figure 4.1). The analysis of the simulation showed the success of the flow generation with the syringe and the needle; however, only the pressure was concluded from the analysis. Hence, the limitation of this flow analysis was denoted by the lack of input data in the simulation to monitor all the possible concentrations and all the possible shear rates effect on the flow of the product. Furthermore, the limitation of the simulation was denoted by crashing of the Horizon platform from the poor RAM of the used computer.

6 CONCLUSIONS AND FURTHER WORK

In the last chapter of the project, the withdrawn conclusions are set below along with the suggested further work. It should be noted that the suggested further work is relying on the researched materials during this project.

6.1 CONCLUSIONS

- The increase in concentration of the Pluronic F127 results in a viscosity increase. However, the increase in shear rates results in a decrease in viscosity related to the sol-gel transition of the hydrogel.
- Pluronic F127 is viable to be applied in drug delivery systems as it fits the properties of temperature and shear stress sensitive hydrogels discussed in the literature.
- Pluronic F127 is viable for drug delivery systems referring to the sol-gel transition at low temperatures as illustrated in this project at 29℃. However, the gelation increase with the increase in viscosity. This allows the Pluronic F127 to be used in drug delivery systems based on the ability to encapsulate the intended drug cells for delivery.
- The shear rates tested in this project on the Pluronic F127 were assed on the final temperature at 40.1℃, which is not the ideal temperature. The ideal temperature should be taken at the average human body temperature range between 36.5 and 37℃.
- The usage of the Poiseuille equation to optimise the pressure drop and the design of the syringe increased the error rate in the pressure measurements. This was addressed by Mezger in this handbook with referring to Bagley

correctio data. The error between the simulation and the calculated pressured drop was at 29.7%, which is high.

- The assumptions taken to design the syringe/needle used for the injection of Pluronic F127 were taken from (Agudo, et al., 2012). The simulation resulted in a pressure through the needle at a maximum of approximately 101000Pa.
- The concentration of the Pluronic F127 at 15% and 20% did not alter the pressure drop in significance values in terms of increasing the shear rates. However, the pressure drop varies at high shear rates with concentrations higher than 25%.

6.2 FURTHER WORK

- Use different concentrations for the Pluronic F128, and mix it with another triblock copolymer to enhance the viscoelastic properties for drug delivery systems.
- Insert the Pluronic F127 input data in the flow simulation as generated from the Excel data sheets taken from the laboratory.
- Optimise the design of the syringe based on simulations made in SolidWorks.

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