A STUDY OF PMMA-CO-MAA PREPARATION USING ULTRASINICATOR VIA TWO STEP SOLVENT EVAPORATION METHOD

Afifah binti Mohd Yassin

J20A0406

A thesis submitted in fulfilment of the requirements for the degree of Bachelor of Applied Science (Materials Tecnology) with Honours

FACULTY OF BIOENGINEERING AND TECHNOLOGY
UMK

2024

DECLARATION

I declare that this thesis entitled "A Study of PMMA-co-MAA Preparation Using Ultrasonicator Via Two Step Solvent Evaporation Method" is the results of my own research except as cited in the references.

Signature: _____

Student's Name: Afifah binti Mohd Yassin

Date: _____

Verified by:

Signature: _____

Supervisor's Name: Dr. Nur Nabilah Binti Shahidan

Stamp: _____

Date: _____

ACKNOWLEGEMENTS

Upon completion of this research, I am grateful to everyone who played a role, big or small, in the completion of this thesis. Your support and encouragement have been invaluable, and I am truly thankful for the opportunity to undertake this academic endeavor.

I would like to express my deepest gratitude to my supervisor, Dr. Nur Nabilah binti Shahidan, for her invaluable guidance, unwavering support, and insightful feedback throughout the entire research process. Your expertise and encouragement have been instrumental in shaping this thesis.

I am also grateful to the member of my thesis committee, Syiqin for their valuable input and constructive criticism. Your perspectives have enriched the quality of this work. Special thanks to UMK lab assistance, Pn Hanisah Izati binti Adli who provided assistance and encouragement during my final year project times. Your camaraderie made the journey more enjoyable and less daunting.

I am indebted to my family especially my mom and dad for their unwavering support, understanding, and patience. Your belief in me has been a constant source of motivation.

Last but not least, I want to thank my self for continuing this research and writing of thesis until finish.

ABSTRACT

Poly (methyl methacrylate-co-methacrylic acid) P(MMA-co-MAA) is biodegradable polymers have a potential to be used in many industries. There is various application such as field of agriculture. cosmetic, detergent, food industry, flavour, pharmaceuticals and painting. Thus, the aim of this study was to investigate the effect of various formulation variables such as effect of water: oil ratio, effect of feeding rate, effect of amplitude of ultrasonicator probe and effect of delay. The preparation method that has been carried out was solvent evaporation method, assisted by high energy input of ultrasonicator probe to obtained smaller particles. The average diameter of particle size and of the microparticles were evaluated and characterized by optical microscope. It was shown that the average particle size increase significantly from 1.48 um to 1.96 um as the water ratio decrease from 70 ml to 10 ml and oil ratio increase from 30 ml to 90 ml. When feeding rate were increased from 0.5ml/ minute for 3:7 and 7:3 water: oil ratio (w: o) to 4 ml/ minute for 3:7 and 7:3 (w: o) the microparticles supposed to be small but the opposite happens, when feeding rate 0.5 ml/ minute for 3:7 (w: o) average diameter for microparticles is 1.6um and increase to 1.8 um for 0.5 ml/ minute for 7: 3 (w: o) compare to 4 ml/ minute for 3: 7 (w: o) average diameter is 1.62 um and increase to 1.68 um for 4 ml/ minute for 7: 3 (w: o). For amplitude, there is three stages of amplitude than have used in this study with is 55%, 70% and 85%. The smaller microparticle is 1.48 um when used 70% of amplitude. While for delay affect when the time of delay increase average size of microparticle also increase, when delay for 1 minute the size average of microparticle is 1.76 um and increase to 2.26 um for 10 minutes. In conclusion, parameter plays major role during preparation of PMMA-co-MAA microparticles, this can provide a range of many kinds of application.

ABSTRAK

Poli (metil methacrylate-co-methacrylic acid) P(MMA-co-MAA) adalah polimer terbiodegradasi berpotensi untuk digunakan dalam banyak industri. Terdapat pelbagai aplikasi seperti bidang pertanian. kosmetik, detergen, industri makanan, rasa, farmaseutikal dan lukisan. Oleh itu, tujuan kajian ini adalah untuk menyiasat kesan pelbagai pembolehubah formulasi seperti kesan air: nisbah minyak, kesan kadar pemakanan, kesan amplitud probe ultrasonicator dan kesan kelewatan. Kaedah penyediaan yang telah dijalankan adalah kaedah penyejatan pelarut, dibantu oleh input tenaga tinggi penyelidikan ultrasonicator untuk mendapatkan zarah yang lebih kecil. Diameter purata saiz zarah dan mikropartikel dinilai dan dicirikan oleh mikroskop optik. Ia menunjukkan bahawa saiz zarah purata meningkat dengan ketara daripada 1.48 um kepada 1.96 um kerana nisbah air berkurangan daripada 70 ml kepada 10 ml dan nisbah minyak meningkat daripada 30 ml kepada 90 ml. Apabila kadar pemakanan meningkat dari 0.5 ml / minit untuk 3:7 dan 7:3 air: nisbah minyak (w: o) hingga 4 ml / minit untuk 3:7 dan 7:3 (w: o) mikropartikel yang sepatutnya kecil tetapi sebaliknya berlaku, Apabila kadar pemakanan 0.5 ml / minit untuk 3:7 (w: o) diameter purata untuk mikropartikel ialah 1.6um dan meningkat kepada 1.8 um untuk 0.5 ml / minit untuk 7: 3 (w: o) berbanding 4 ml / minit untuk 3: 7 (w: o) diameter purata ialah 1.62um dan meningkat kepada 1.68um untuk 4 ml / minit untuk 7: 3 (w: o). Untuk amplitud, terdapat tiga peringkat amplitud daripada yang digunakan dalam kajian ini dengan 55%, 70% dan 85%. Mikropartikel yang lebih kecil ialah 1.48 um apabila digunakan 70% amplitud. Manakala untuk kelewatan menjejaskan apabila masa kelewatan meningkatkan saiz purata mikropartikel juga meningkat, apabila kelewatan selama 1 minit purata saiz mikropartikel adalah 1.76 um dan meningkat kepada 2.26 um selama 10 minit. Kesimpulannya, parameter memainkan peranan utama semasa penyediaan mikropartikel PMMA-co-MAA, ini boleh menyediakan pelbagai jenis aplikasi.

Table of Contents

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

PMMA-co-MAA	Poly (methyl methacrylate-co-methacrylic acid)
PVA	Polyvinyl Alcohol
DCM	Dichloromethane

LIST OF SYMBOLS

g/mol	Gram per mo
µm	Micrometre
o/w	Oil in water emulsio
Dv	Range diameter
wt%	Weight percentag

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Small particles with a size ranging from a few nanometers to a few micrometres are referred to as microparticles (Yu et al., 2009). Biodegradable polymers are one of the materials that have been used during the preparation of microparticles due to their high biocompatibility for each polymer that has been selected (Bile et al., 2015). Over the past few years, polymer microparticles have also manage to attract worldwide attention due to the properties of biodegradable polymers that can be offered (Siepmann et al., 2006). In several disciplines, microparticles can be used in many different applications including health, environmental science, materials science, and technology, microparticles can be either natural or artificial (Yu et al., 2009).

Encapsulation (hollow and solid) is the process of placing medications or active substances inside of a carrier material. This carrier serves as a protective shell that can improve the stability, solubility, or bioavailability of the encapsulated material. It frequently takes the form of microparticles. Targeted delivery can be made possible via encapsulation, allowing the drug to be released over a predetermined length of time or at a particular location in the body (Rivas, C et al., 2017).

Hollow encapsulation are polymeric spheres with a single pore inside the particle. On the other hand, polymers with many pores are called porous polymers. Concentration in hollow encapsulation has increased steadily over the past few decades because it can readily be used

to upload drugs and active species and can efficiently attach to special target molecules into the hollow interiors by chemical modification. They enable controlled and targeted release by being able to encapsulate pharmaceuticals and deliver them to a particular body (Ramli, R. A et al., 2017). Other examples of solid microparticles are, they can be employed as fillers or additives in materials science and technology to enhance a material's strength, conductivity, or optical qualities. In fields like cosmetics, where they can produce desired effects like texture or colour, microparticles are also used (Malikmammadov et al., 2018).

In this study section Poly (methyl methacrylate-co-methacrylic acid) was used to prepare the microparticle through the solvent evaporation method using ultrasonicator probe. Methacrylic acid (MAA) and methyl methacrylate (MMA) are the monomers that make up the hydrophobic polymer known as poly (methyl methacrylate-co-methacrylic acid), also known as PMMA-co-MAA. The polymer's characteristics, including its glass transition temperature, inherent viscosity, and concentration of surface carboxyl groups, can be managed by adjusting the ratio of MMA to MAA.

1.2 Problem Statement

Hence, the purpose of this research is to provide a background study in the microparticles further application. This study can be done by optimizing the parameter such as concentration of polymer, molecular weight of polymer, oil phase amplitude and pulse of ultrasonictor probe by using solvent evaporation methods. More than that, solvent evaporation method is by far the most commonly used for producing microparticles with different parameter due to the simple equipment (Cortez et al., 2018) and has been assisted by ultrasonicator probe for a better result. Furthermore, here is not much clear understanding of

the effect of ultrasonicator on the preparation of PMMA-co-MAA via two-step solvent evaporation method for future study.

1.3 Research Objectives

The objectives of this study will be as follows:

1. To prepare PMMA-co-MAA microparticles via ultrasonicator probe assisted by solvent evaporation method using different parameters such as effect of Water: Oil ratio, effect of feeding rate and effect of amplitude for PMMA-co-MAA.
2. To characterize the size of PMMA-co-MAA microparticles with different parameters using optical microscope and scanning electron microscope.

1.4 Scope of Study

In this study poly (methyl methacrylate-co-methacrylic acid) P (MMA-co- MAA) was selected use within solvent as oil phase by w/o emulsion to obtain microparticles. At the 0.3g of 34 000 kg/mol PMMA-co-MAA and 30ml of DCM (1%wt) oil phase was prepared, to water phase was prepared at 0.35g and 70ml of distilled water (0.5%wt). Each different parameters of oil phase and water phase indicates as significant impact to obtain characteristic of microparticles. Additionally, the solvent of choice has a role in how well the microparticles are prepared. Finally, microparticles is characterized by using optical microscope.

1.5 Significance of Study

The factors that affect the size and surface morphology of PMMA microparticles from different polymer concentration, different PMMA molecular weight and different oil phase ratio seem to be worth identifying in order to design microparticles with the desired profile. As a result, the varied microparticle sizes that have been produced can be used for various applications.

CHAPTER 2

LITERATURE REVIEW

2.1 Microparticle

Microparticles in drug delivery refer to small solid particles with a size typically ranging from 1 to 100 micrometres (μm) that are designed to encapsulate and deliver therapeutic agents such as drugs, proteins, or genetic material to targeted sites in the body. A drug delivery system, it is offers numerous advantages based on their structural and functional abilities, and their application is suitable for convenient and tolerable drug administration via several routes. They can be included in a variety of pharmaceutical dosage forms, including solids (capsules, tablets), semisolids (gels, creams, pastes), and liquids (solutions), depending on the formulation (Lengyel et al., 2019). Two types of microparticle are going be highlighted such as microspheres and microcapsules.

Microspheres are made up of tiny, spherical particles having a solid outer shell. They don't hold any fluid because they are hollow. Polymers are used to make these particles. Microspheres usually have a size between 1 μm and 1 mm. Microspheres' large surface area and small particle size make them popular in medication delivery applications. They can be administered by a number of techniques, including transdermal, nasal, ophthalmic, and parenteral routes. Proteins, peptides, antibodies, antigens, and other tiny molecules can bind to microspheres, which enables them to pass through the body and deliver medications at precise times. Microcapsules are spherical in shape as well, however they differ slightly in structure.

They are composed of a shell-like coating covering a membrane-enclosed core. There may occasionally be more than one core in the coating. A pharmacological component, stabilisers, or additives are found in a microcapsule's core. An inert polymer, colouring agents, plasticizers, resins, waxes, and lipids make up the outside layer. They enable the core to be kept apart from the outside world and released as needed. Sustained medication release. preserving medications that are light, moisture, or oxygen sensitive (Ilhan, M et al., 2024). In summary, the key difference lies in the structure. Microspheres have solid outer casing, hollow inside but microcapsules have solid or liquid core within a shell-like coating. Both microspheres and microcapsules serve similar goals for controlled drug release, but their distinct structures make them difference (Experts, C. M. et al., 2021).

2.1.1 PMMA-co-MAA

Methacrylic acid (MA) and methyl methacrylate (MMA) are the two monomers that make up the copolymer known as PMMA-co-MA. Poly (Methyl Methacrylate-co-Methacrylic Acid) is what the abbreviation stands for. Methacrylic acid (MA) is a comonomer that is added during the copolymerization process, giving the PMMA matrix acidic characteristics. The solubility, thermal stability, and surface reactivity of the resultant copolymer can all be altered as a result (Deka, N et al., 2022)

Due to its unique characteristics and numerous uses, PMMA-co-MA has demonstrated a great deal of potential recently. PMMA-co-MAA is a low-cost polymer that has great impact resistance, flexibility, low specific weight, and chemical inertness. Enzymes, DNA, proteins, and metal particle deposition have all been effectively immobilised using PMMA-co-MAA for diagnostic reasons (Hosseini, S et al., 2014)

2.2 Application of microparticle

The reasons size of microparticles matters are because microparticles can be utilised as drug delivery agents, and their size can have an impact on their drug loading potential, release characteristics, and targeting effectiveness. While larger microparticles can offer sustained drug release and better targeting to particular tissues or cells, smaller microparticles can offer more surface area for drug loading and faster release kinetics. Qualities flow of microparticles', flow characteristics, such as their capacity to move via narrow channels or injectors, might vary depending on their size. For some applications, including microfluidics or injectable formulations, smaller microparticles may offer better flow characteristics (Lengyel et al., 2019). Furthermore, there are many more applications of microparticles besides medicine such as food, agriculture and the cosmetic industry.

The application of new technologies in the food industry has been highly researched in the last few decades to obtain benefits in terms of safety, health, and products with high quality. Microparticle is a science that offers favourable conditions and qualities for applications in this specific industry and other industries, providing a good alternative for control and food production (Bareras-Urbina et al., 2016). The application of microparticles using microencapsulation in agriculture, are focused on the preparation of complex biopolymer based microparticles. The benefits conferred by encapsulation include the slow release of the bioactive ingredient, more efficient exploitation of the chemical, greater safety for the user, and better protection of the environment (Vinceković, M et al., 2019)

In the cosmetic industry, most peeling products (exfoliators) available on the market, used in cosmetic and aesthetic dermatology applications, contain synthetic microbeads as abrasive agents. These non-biodegradable microparticles have a negative effect on the

environment after being discharged into it, especially on aquatic ecosystems. Microbeads made of biopolymers could be used as an alternative to synthetic beads. Using the encapsulate, spherical sodium alginate microparticles and a combination of sodium alginate and starch were produced. Similar to commercial synthetic balls, sodium alginate-based microparticles have an impact on the skin. In addition, they are entirely natural, biodegradable, and environmentally beneficial substances, which makes them a desirable substitute for synthetic microplastics, which are frequently used (Kozlowska, J et al., 2019)

2.3 Method

Spray drying, hot melt and solvent evaporation methods are two of the processing methods for microparticles that have been suggested by earlier research. The technique specification, benefits, and limitations of such preparation methods have been covered in the section below.

2.3.1 Spray drying method

For encapsulation, spray-drying (Figure 2.1) of microparticles has been extensively researched. This method has several benefits, including the ability to be operated, use for hydrophobic medicines, and suitability for the mass manufacturing of microparticles. These reasons have led to the widespread usage of spray drying technology in industrial processes that involve drying and particle production. When the final product must adhere to exact quality criteria for particle size distribution, residual moisture content, bulk density, and particle form, spray drying is the best procedure (Rastogi et al., 2016).

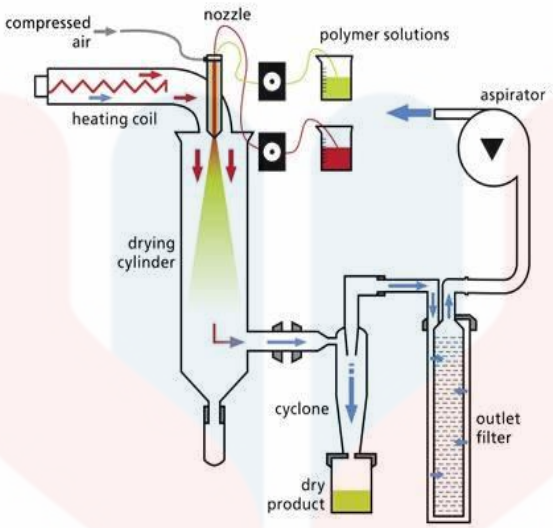


Figure 2.1: Diagram of spray drying process (Source: Rastogi et al., 2016).

Additionally, this approach can avoid the problem of emulsion-based approaches producing significant amounts of solvent-contaminated water phase. Spray drying is more difficult on a small bench scale or when the amount of medicine is constrained in the early phases of the creation of the microparticles formula since higher batch sizes are often needed as opposed to the solvent evaporation procedures. (Wischke et al., 2008).

2.3.2 Hot melt method

For microencapsulation particles, the hot melt method (Figure2.2) of particle production is best. By using this technique, a water-soluble polymer that is immiscible with the matrix polymer can be used to disperse the matrix polymer. After dissolving the water-soluble polymer in water, the particle emulsion will then cool and solidify, and the matrix polymer microencapsulation particles will be recovered. Another method of encapsulating medicines into biodegradable polymers without the use of organic solvents is by melting procedures,

which call for the dispersion or melting of the drug in the polymer melt. According to previous study, the hot treatment of the medicine and the numerous processes required to produce smooth microparticles are the constraints of the melting technique (Hossain et al., 2015).

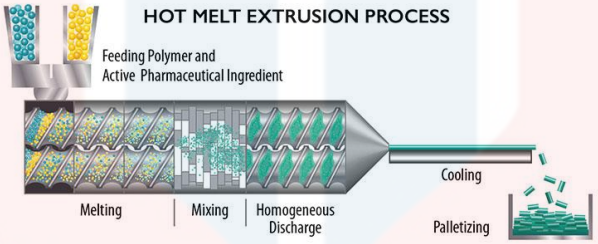


Figure 2.2: Hot melt method (Source: Southwest, R, I, et al., 2021)

2.3.3 Solvent evaporation method

For this study solvent evaporation methods are used. A variety of biocompatible polymers, including poly (methyl methacrylate-co-methacrylic acid) P (MMA-co- MAA), have been utilised to successfully create microspheres using the emulsion solvent evaporation technique, which was fully developed at the end of the 1970s. Because it just needs mild conditions like ambient temperature and continual stirring, the emulsion solvent evaporation technique is favoured to other preparation methods like spray drying, sonication, and homogenization. As a result, a stable emulsion can be created without affecting the emulsion effectiveness. A variety of processing and material parameters are used in the general emulsification solvent evaporation method to create nanoparticles, including the amount of energy used, the power and duration used, the volume of the aqueous phase, the concentration of polymers and the molecular weight and end groups of the polymers, the volume of the solvent, and the concentration of surfactants. The size and/or drug content of the microparticles are influenced by each of these processing and material characteristics (Hoa, L et al., 2012)

2.4 Instrumentation

Ultrasonicator and homogenaizer are two of the machines to make microparticles that have been suggested by earlier research.

2.4.1 Homogenaizer

In order to create an even, homogenous mixture, a homogenizer is a sort of mixer that pushes material through a tiny, limited aperture. A homogenizer is a type of mixer that forces material through a small opening to produce a homogeneous mixture. It uses a variety of forces, such as cavitation, turbulence, and high pressure, to distribute a solution's contents uniformly. Homogenizers are used for emulsification, suspension, grinding, dispersing, and dissolving in addition to mixing. Some of the functions of homogenizer is microbial inactivation, emulsification and particle size reduction. Homogenizers use pressure, turbulence, and cavitation to create uniform mixtures, making them essential in various industries and scientific applications (Lee, H et al., 2012).

2.4.2 Ultrasonicator

An ultrasonic homogenizer or sonicator, employs high-frequency sound waves to disperse particles and create a homogenous mixture. It is frequently employed for a variety of purposes, including sample preparation, cell disruption, and emulsification, in the domains of the life sciences, chemistry, and materials science. Ultrasonicators function by transforming electrical energy into high-frequency sound waves that travel through a liquid medium via a transducer. Cavitation, which is the development and dissolution of small bubbles in the liquid, is brought on by sound waves. High shear forces are produced when these bubbles burst,

breaking up the particles and distributing them more uniformly throughout the mixture. (Ultrasonics, H et al., 2023).

Both homogenizers and ultrasonicators can effectively reduce particle size and produce homogenous mixes and dispersions. However, compared to homogenizers, ultrasonicators have a number of benefits. While homogenizers use mechanical force, such as high-pressure pumps or rotors, which can increase the risk of contamination due to component wear and tear, ultrasonicators use high-frequency sound waves to create shear forces that break down particles. Less heat produced, ultrasonicators produce less heat than homogenizers, which is beneficial for samples that are sensitive and could be harmed by high temperatures (Labrotovap et al., 2020).

CHAPTER 3

MATERIALS AND METHODS

3.1 Materials

Poly (methyl methacrylate-co-methacrylic acid) average Mw-34,000 by GPC, average Mn-15,000 by CPG, Polyvinyl Alcohol (PVA), Tween 80, Dichloromethane 84,93 g/mol (DCM), Acetone, distilled water. All materials has been purchased from Sigma-Aldrich, Germany.

3.2 Methods

In this study, microparticles were prepared using solvent evaporation method via an ultrasonicator. To find out how different parameters affected the size of the microparticles, a number of parameters were changed.

3.2.2 Preparation of microparticle

The following describe, a 1:9 volume ratio between the oil and water phases of an o/w emulsion sample. The oil phase contains 0.3g of 34 000 kg/mol PMMA-co-MAA and 30ml of DCM (1%wt), 1 ml will be added into the water phase that contains 0.35g and 70ml of distilled water (0.5%wt) using a syringe pump. This immiscible solution undergoes an emulsification process by using high energy input of an ultrasonicator probe with 70% amplitude. The employed pulse is a 5 second run, 5 second pause cycle. After the microparticles emulsion solution was produced, the solution would be placed in a rotary evaporator. There were a number of parameters that were altered during the processing of PMMA-co-MMA microparticles, including the PMMA-co-MAA concentration (0.2g, 0.5g, 1.0g, 1.5g, 2.0g, and

2.5g), PMMA molecular weight (34 000kg/mol and 15 000kg/mol), oil phase volume fraction (1:9, 3:7, 5:5, 7:3, and 9:1), ultrasonicator probe amplitude (40%, 80%, 60%), and pulse of ultrasonicator probe (5 sec run/5 sec stop and 3 sec run/1 sec stop) of ultrasonicator probe during preparation of PMMA-co-MAA microparticles (Table 3.1) For the evaporation process, rotary evaporator has been used to control the evaporation rate of solvent during evaporation process, rotary evaporator that has been used was at 95 rpm speed for 20 minutes at room temperature (25°C).

Amount of PMMA-co-MAA (g)	0.2g, 0.5g, 1.0g, 1.5g, 2.0g, and 2.5g
Oil phase in ratio	1:9, 3:7, 5:5, 7:3, and 9:1
Amplitude of ultrasonicator probe (%)	40%, 80%, 60%
Pulse of ultrasonicator probe (sec)	5 sec run/5 sec stop and 3 sec run/1 sec stop

Table 3.1: Table of parameter used in lab.

3.3.1 Optical Microscope

Optical Microscope has been used to observe microparticles solutions. Firstly, connect a power supply to the light microscope. The lowest objective lens should be in place by rotating the revolving nosepiece. One drop of PMMA microparticle solution was mixed with one drop of distilled water for the preparation technique of the sample before being seen through an optical microscope, and it was then applied to the top of the glass slide using a dropper. Look into the eyepiece and slowly rotate the coarse adjustment knob to bring your specimen to focus. To effectively evaluate the picture of the emulsion microparticles, the observation procedure will start with lesser magnification (4x magnification) and move up to greater magnification (40x magnification).

Then, an image that was acquired using image analysis software and calculated to contain between 450 and 500 microparticles was used for the microparticle size study.

CHAPTER 4

RESULT AND DISCUSSION

4.1 Size and morphology of PCL microparticles

This chapter discussed the results obtained from various parameters, namely the size of PMMA-co-MAA microparticles. The aim was to determine the effect of parameters on the size of PMMA-co-MAA microparticles that were affected due to changes in these parameters.

In Table 4.1 was shown the average diameter of microparticle that have been obtained from different concentration of ratios water to oil phase, feeding ratio, and amplitude. In this characterization process, 40x magnification image of microparticles that have been observed under optical microscope will be calculated and analysed.

Table 4.1: Size PMMA-co-MAA microparticle

Sample	Water: Oil Ratio	Feeding Rate (ml/min)	Amplitude (%)	Concentration of surfactant (wt%)	Average diameter (Dv) (µm)
1:9(2ml/min)70%	1:9	2ml/min	70%	1	1.96
3:7/(2ml/min)/70%	3:7	2ml/min	70%	1	1.76
5:5/(2ml/min)/70%	5:5	2ml/min	70%	1	1.54
7:3/(2ml/min)/70%	7:3	2ml/min	70%	1	1.48
3:7/(2ml/min)/55%	3:7	2ml/min	55%	1	2.02
5:5/(2ml/min)/55%	5:5	2ml/min	55%	1	1.84
7:3/(2ml/min)/55%	7:3	2ml/min	55%	1	1.72
3:7/(2ml/min)/85%	3:7	2ml/min	85%	1	1.74
5:5/(2ml/min)/85%	5:5	2ml/min	85%	1	1.62
7:3/(2ml/min)/85%	7:3	2ml/min	85%	1	1.54
3:7/(0.5ml/min)/70%	3:7	0.5ml/min	70%	1	1.6
3:7/(4ml/min)/70%	3:7	4ml/min	70%	1	1.62
7:3/(0.5ml/min)/70%	7:3	0.5ml/min	70%	1	1.8
7:3/(4ml/min)/70%	7:3	4ml/min	70%	1	1.68

4.2 Effect of Water: Oil ratio for PMMA-co-MAA microparticle size

From Figure 4. 2, trend for size of PMMA-co-MAA microparticles has shown that the size of PMMA-co-MAA microparticles were depending to the amount of PMMA-co-MAA, when the number of PMMA-co-MAA increases, average diameter of microparticles that have been obtained also has been increases.

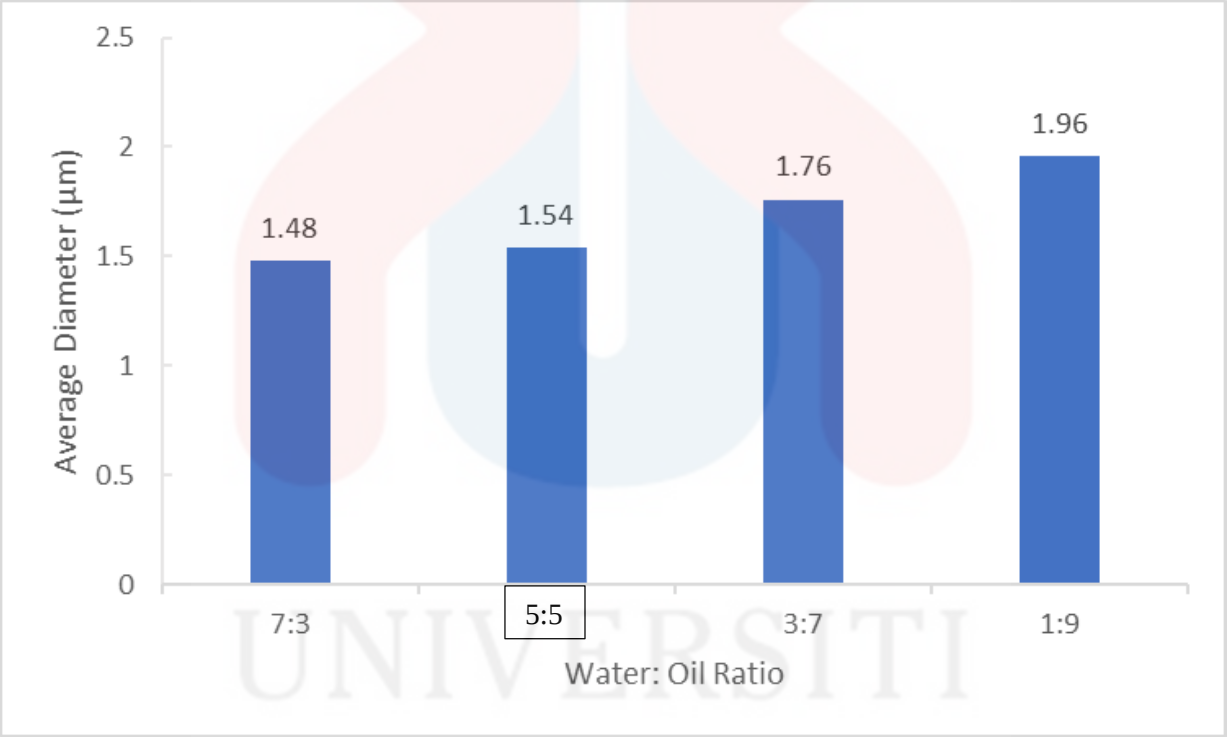
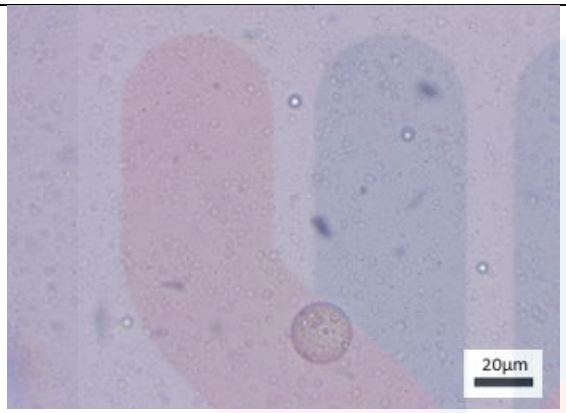
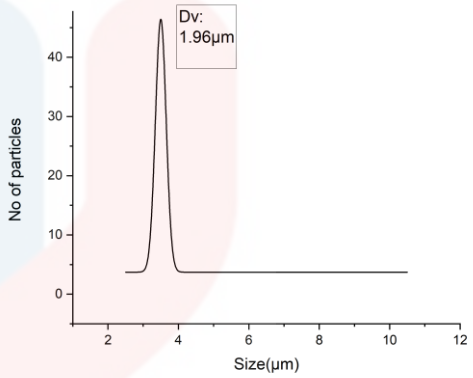
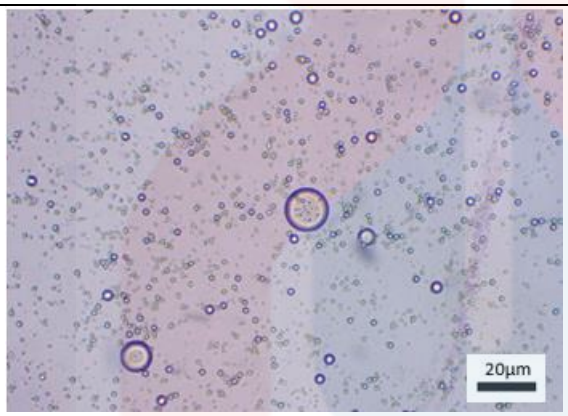
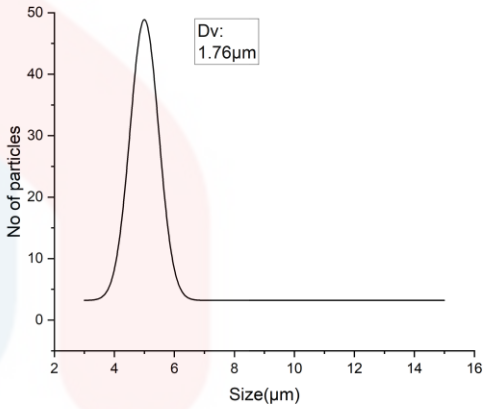
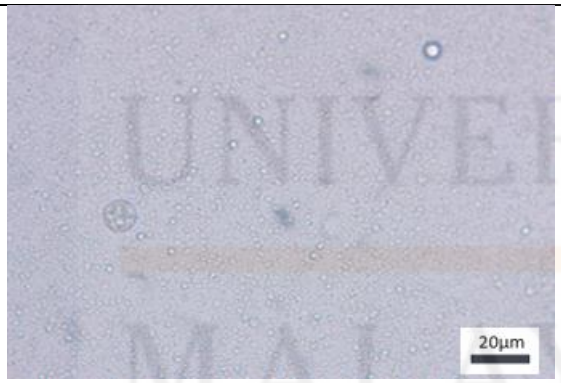
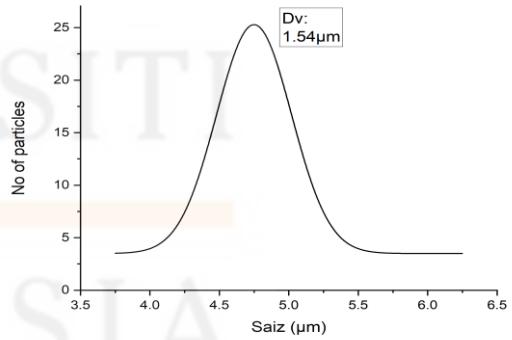


Figure 4.1: Average diameter of PMMA-co-MAA microparticles effect from different amounts of water: oil ratio.

Figure 4.1 for graph average diameter of PMMA-co-MAA microparticles effect from different amounts of water: oil ratio. shows the trend with is size of microparticle increase from 1.48um for water: oil ratio 7: 3 to 1.96um for water: oil ratio 1:9. This can be explained that increase of concentration polymer indicates in viscosity of oil phase result in less absorption layers of surfactant for diffusion to particles forming. On the other hand, low polymer concentration indicate that low viscosity could result in strong absorption layer of surfactant to forming small particle Francis et al., (2011).

The increasing size of PMMA-co-MAA microparticles from 7:3 to 1:9 water: oil ratio could be attributing to the present of ratio water: oil that has been used in this experiment. The larger size that has been obtained when oil phase is increases was corresponded to the higher amount solution of DCM and lower amounts of PVA in 1:9 oil phase in volume fraction has increases the coalescence process between particles and slower the degradation process of solvents. Previous research Kemala et al., (2012) also has showed that, surfactant plays a major role during formation of emulsion microparticles. PVA also has been proven from previous study as, its ability to reduce coalescence between microparticles by lowering the interfacial tension, which reduce the resistance for droplet to deformation and formed smaller size of microparticles. According to Mohammed et al., (2016) at low oil phase, the number of particles increases and produces a narrow particle size distribution, compared to high volume fractions resulting in a wide particle size distribution.

Water: oil ratio	Emulsion microparticles of PMMA-co-MAA (40xmagnification)	Graph for size distribution of emulsion of PMMA-co-MAA
1: 9		
3: 7		
5: 5		

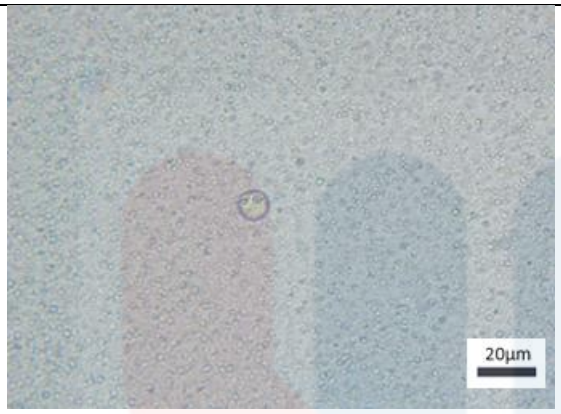
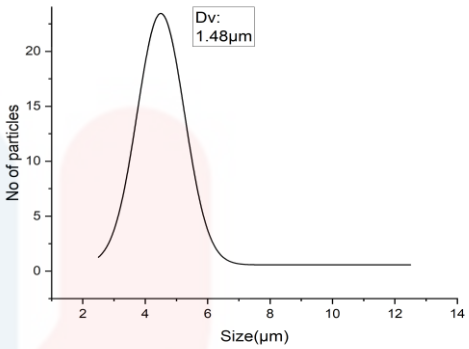
7: 3		

Figure 4.2: Effect of different water: oil ratio of PMAA-co-MAA emulsion microparticle

4.3 Effect of feeding rate for PMMA-co-MAA microparticle size

From Figure 4.3, shown the effect of feeding rate to the average size of microparticle for 0.5mil/minute to 4mil/minute using 3:7 and 7:3 water: oil ratio. Result average diameter for 0.5mil for 3:7 water: oil ratio (w: o) is 1.6um and continued to rise to 1.62um for feeding 4mil for 3:7 (w: o) there was an increase from 0.02um, for feeding 4mil for 7:3 (w: o) average diameter was 1.68um there was an increase to 0.06um. The increase in average diameter indicates a positive increase according to previous studies that short feeding times yield bigger particle sizes. Helmiyati at el., (2008).

Emulsification process is increased when the feeding rate time is decreased. Different feeding times were used over the course of this lab section it was observed that short feeding times yield bigger particle. This was consistent with research by Bao et al., (2004) who found that short feeding times result in larger particle size. Two steps feeding process was used where the first is for the prepare oil phase 0.3g of 34000kg/mol PMMA-co-MAA and 30ml of DCM and prepare water phase (0.35g PVA and 70ml of distilled water (0.5%)). The results of the average diameter of PMMA-co-MAA microparticles effected from different amounts of feeding time are given in figure 4.3.

Graph average diameter of PMMA-co-MAA microparticles effected from different amounts of feeding rate time has shown a significantly difference from previous result and discussion for 0.5mil for 7:3 (w: o), where when the long feeding rate time will form a smaller particle but vice versa the result shown large microparticles and non-uniform size of microparticles has formed. This happens as a result of a 6-minute delay before the evaporation process occurs.

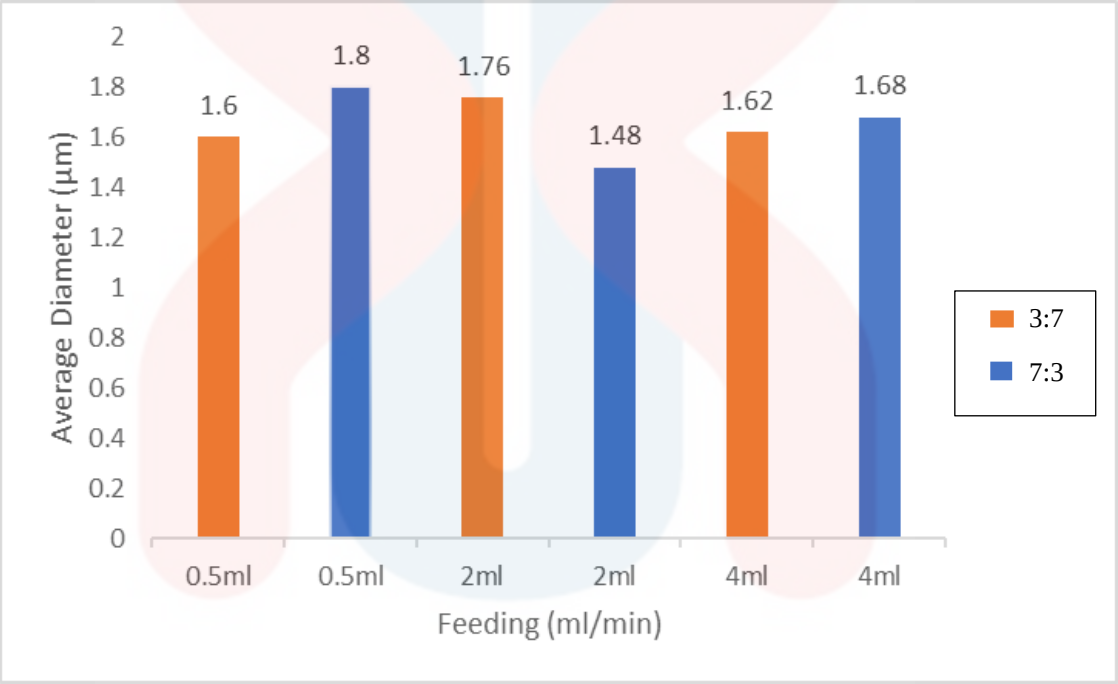
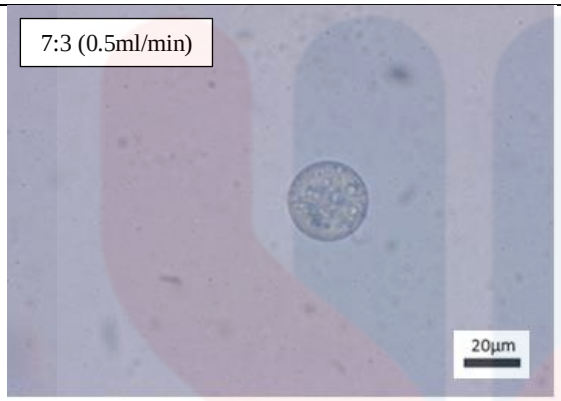
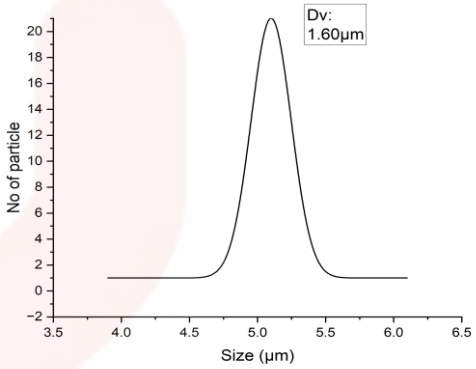
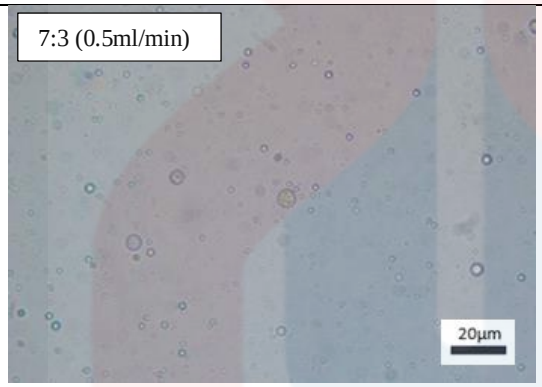
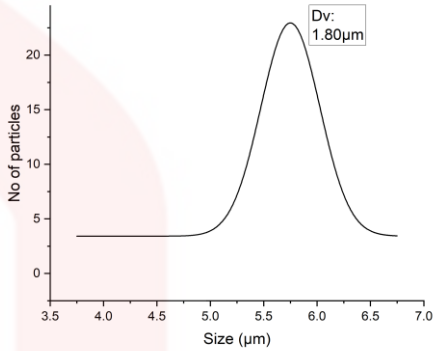
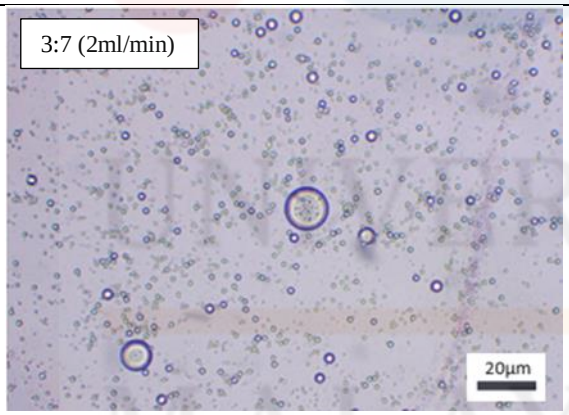
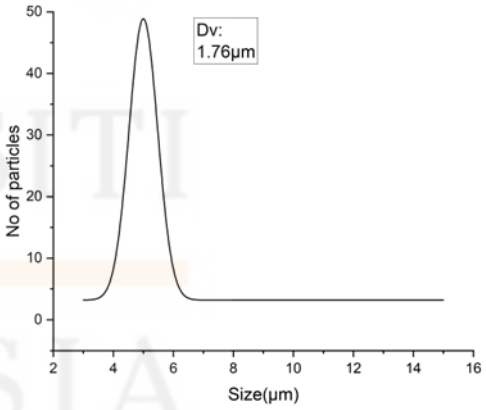


Figure 4.3: Average diameter of PMMA-co-MAA microparticles affected from different amounts of feeding time.

Feeding rate	Emulsion microparticles of PMMA-co-MAA (40xmagnification)	Graph for size distribution of emulsion of PMMA-co-MAA
0.5ml		
0.5ml		
2ml		

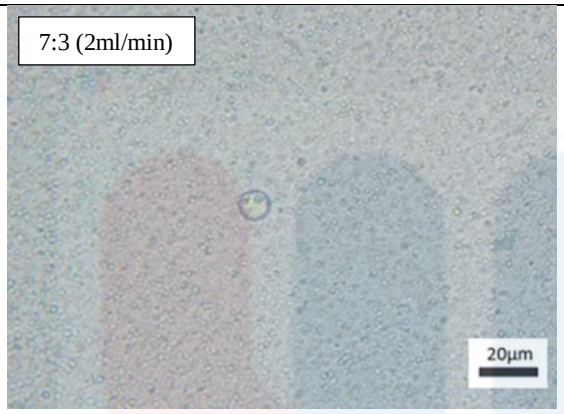
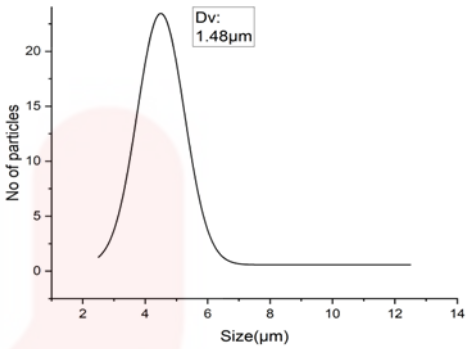
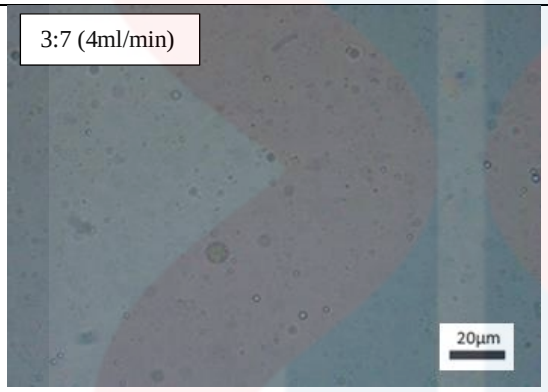
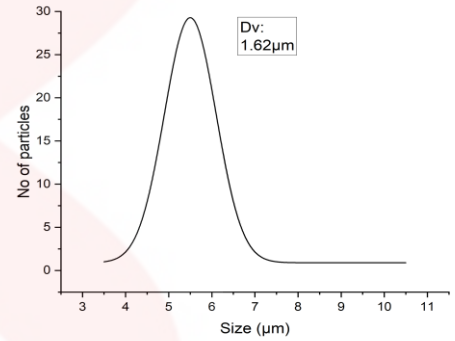
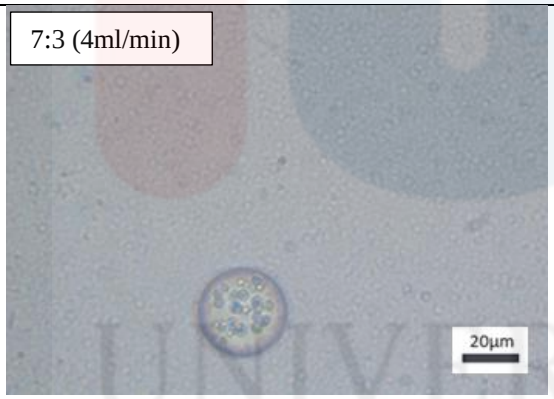
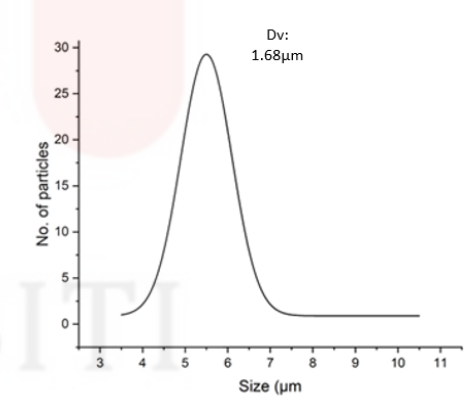
2ml		
4ml		
4ml		

Figure 4.4: Effect of feeding for PMAA-co-MAA emulsion microparticle

4.4 Effect of amplitude for PMMA-co-MAA microparticle size

Figure 4.5, shown the effect of amplitude to the average size of microparticles for 55%, 70% and 85% amplitude emulsification process amplitude of ultrasonicator was increased.

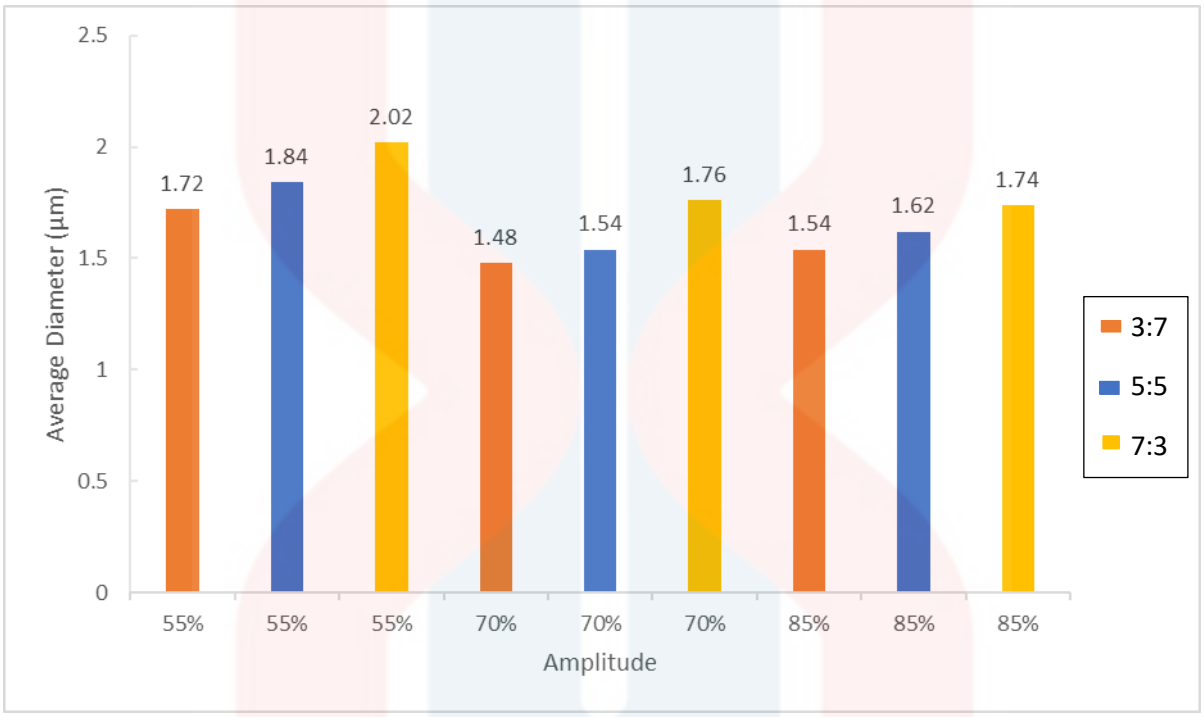


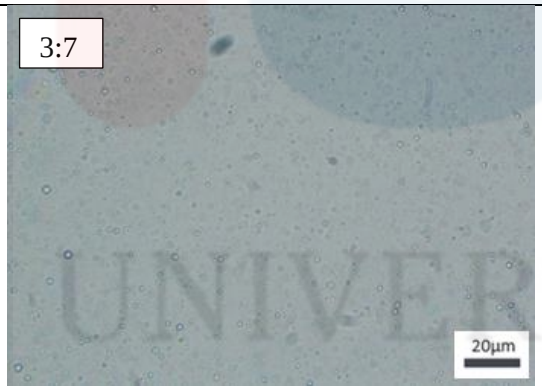
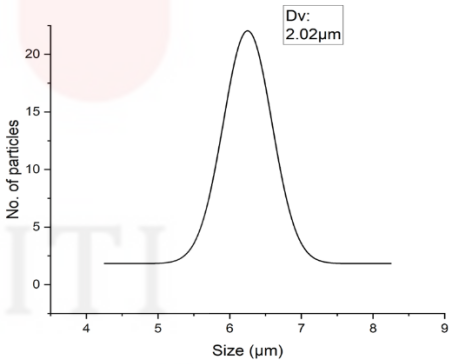
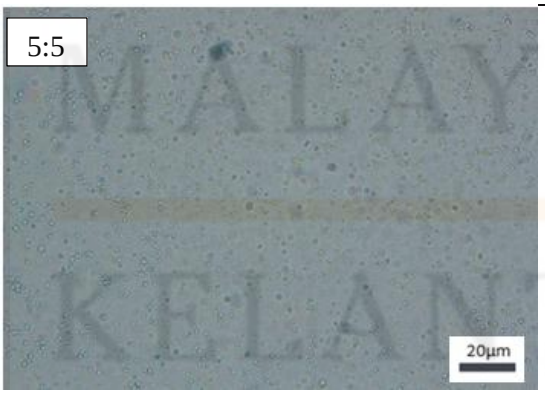
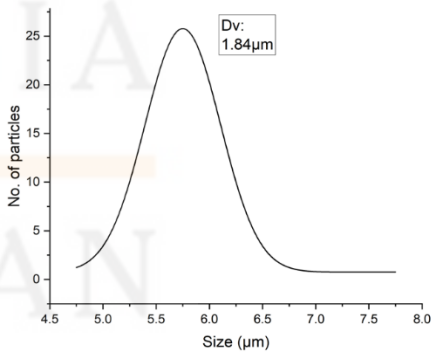
Figure 4.5: Average diameter for PMMA-co-MAA microparticles that has affected for 55%, 70% and 85% of amplitude

For figure 4.5, as can be seen the average size of microparticles will be increased with an increasing the percentage amplitude of ultrasonicator probe from 55% to 70% to 85%. The discovered finding was consistent with earlier research that carried out by Cucheval et al., (2008), it has reported that the rate of size reduction can be increased by increasing the power input of ultrasonicator probe (Cucheval & Chow, 2008). This could be the result of applying high energy input when using a high percentage amplitude.

When pressure of amplitude increased from 55% for 3:7 (w: o) to 70% for 3:7 (w: o) to 85% for 3:7 (w: o) the average microparticle decreased from 2.02um to 1.76um to 1.74um decrease about 0.26um and 0.02um. When pressure of amplitude increased from 55% for 5: 5 (w: o) to 70% for 5: 5 (w: o) to 85% for 5: 5 (w: o) the average microparticle decreased from

1.84um to 1.54um to 1.62um decrease about 0.3um and 0.12um. When pressure of amplitude increased from 55% for 7: 3 (w: o) to 70% for 7: 3 (w: o) to 85% for 7: 3 (w: o) the average microparticle decreased from 1.72um to 1.48um to 1.54um decrease about 0.24um and 0.06um.

Thus, it shown that when there is high shear stress it may lead to small particles size compare to low shear stress. This factors also has proved previous statement from Bile et al., (2014) that has been mention in parameter amounts of PMMA-co-MAA, where higher shear force is able to break the attractive force between oil droplets hence smaller size of microparticles was able to produced. Gaikwad et al., (2008) also discovered that an increase in amplitude power causes an increase in the applied sound's pressure amplitude, which intensifies the cavitation occurrence.

Amplitude	Emulsion microparticles of PMMA-co-MAA (40xmagnification)	Graph for size distribution of emulsion of PMMA-co-MAA
55%		
55%		

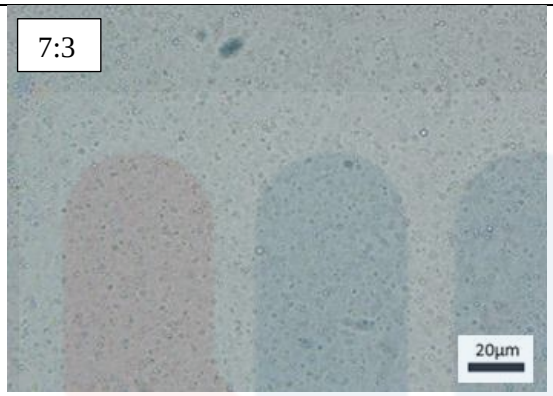
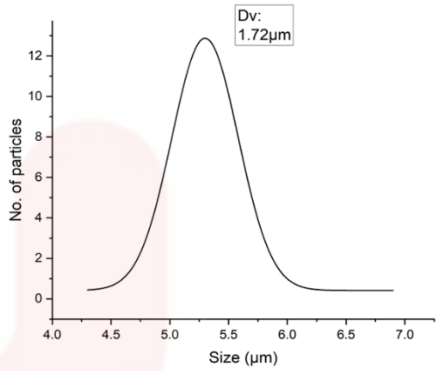
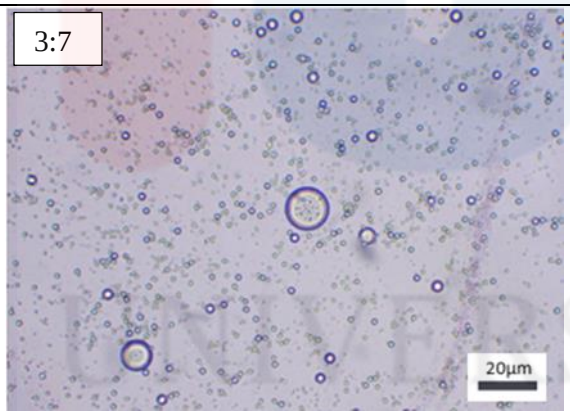
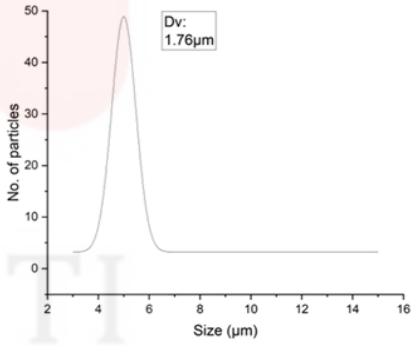
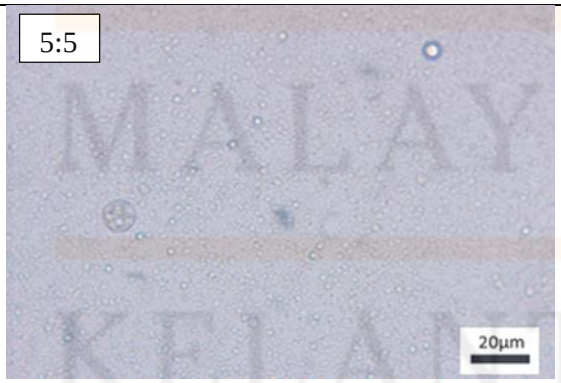
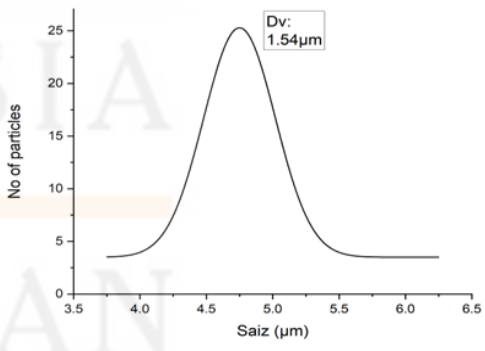
55%		

Figure 4.6: Effect of amplitude (55%) during emulsification process of PMMA-co-MAA emulsion microparticles

Amplitude	Emulsion microparticles of PMMA-co-MAA (40xmagnification)	Graph for size distribution of emulsion of PMMA-co-MAA
70%/3: 7		
70%		

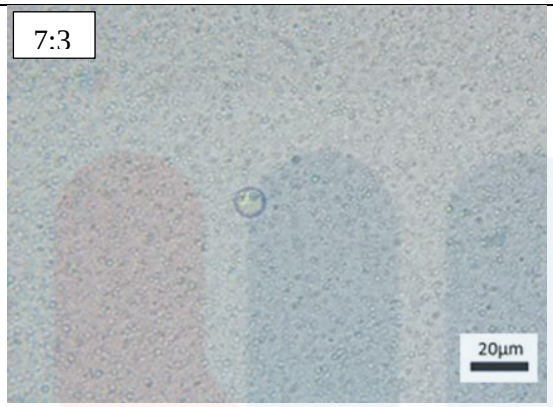
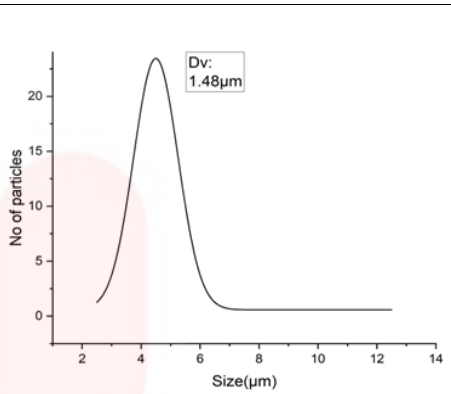
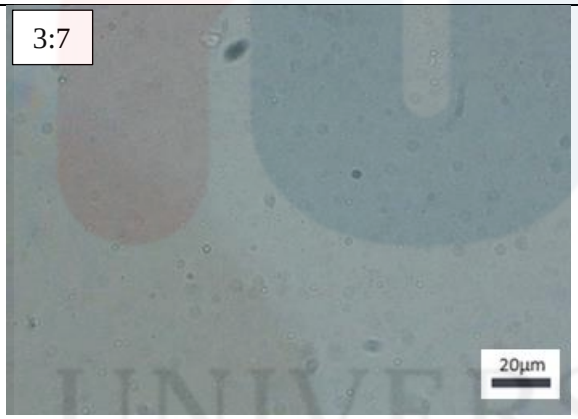
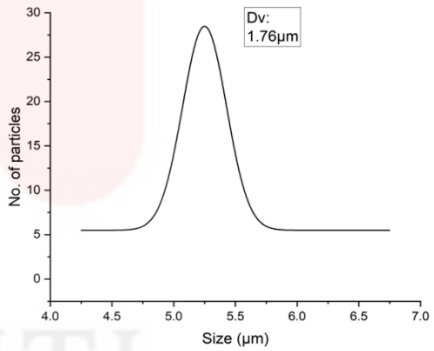
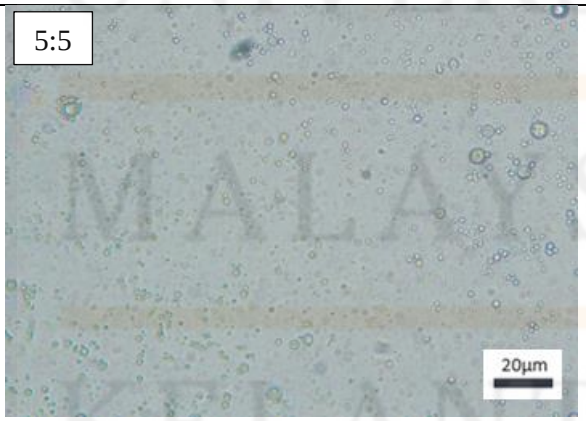
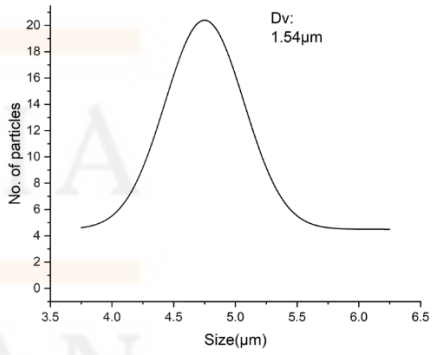
70%		

Figure 4.7: Effect of amplitude (70%) during emulsification process of PMMA-co-MAA emulsion microparticles

Amplitude	Emulsion microparticles of PMMA-co-MAA (40xmagnification)	Graph for size distribution of emulsion of PMMA-co-MAA
85%		
85%/ 5: 5		

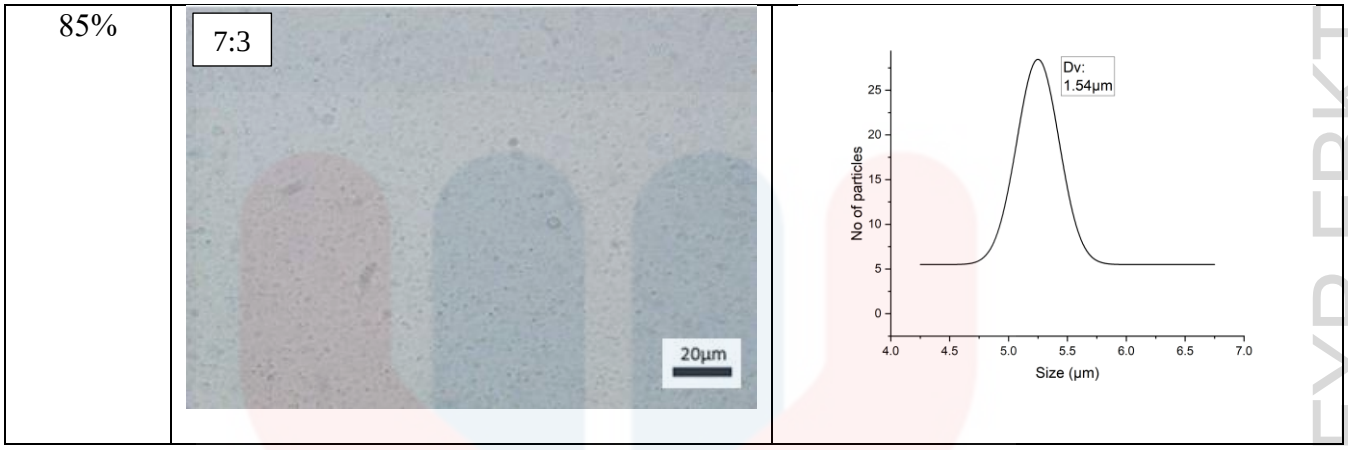


Figure 4.8: Effect of amplitude (85%) during emulsification process of PMMA-co-MAA emulsion microparticles

4.5 Effect of delay for PMMA-co-MAA microparticle size

Figure 4.9 shown the effect of average diameter for PMMA-co-MAA microparticles that has affected time of delay. When the time of delay increase, average of microparticle also increase.

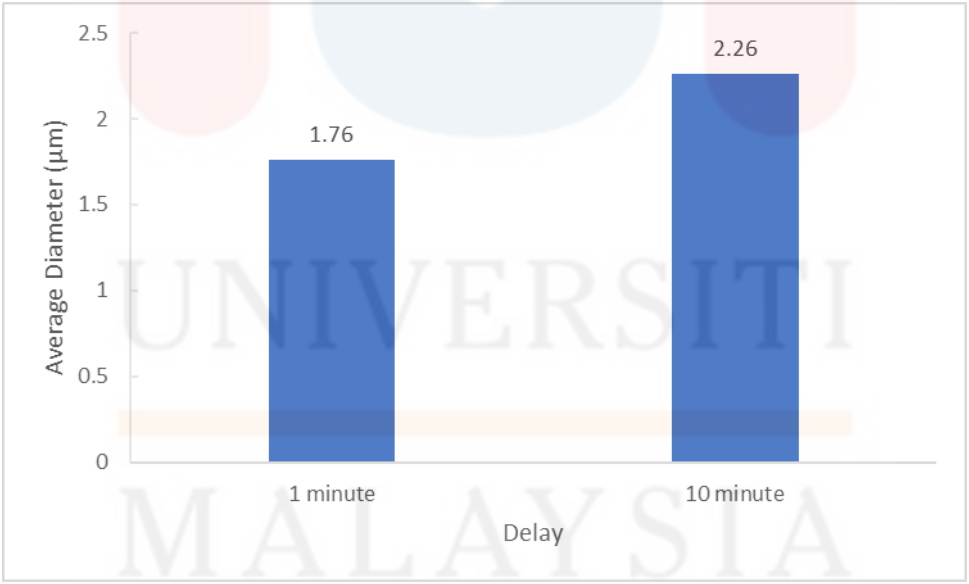
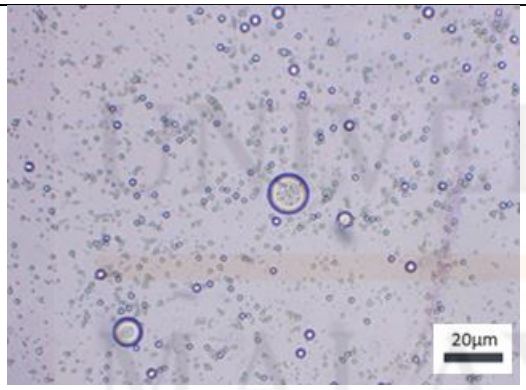
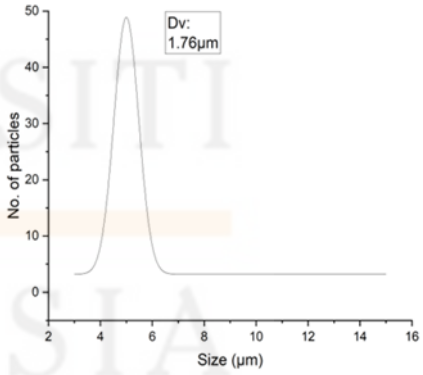


Figure 4.9: Average diameter for PMMA-co-MAA microparticles that has affected time of delay

Figure 4.9 shows the delay effect on average diameter for PMMA-co-MAA microparticles. The 10 minutes delay prior to evaporation shows an increase in the average

diameter size of the PMMA-co-MAA microparticles. During the delay, two or more droplets may merge to form a larger droplet and it is called the coalescence process. Geri, M., et al., (2017), which can lead to a shift in the size distribution of the particles. The extent of this shift depends on various factors such as the size of the particles, the rate of coalescence, and the conditions under which the coalescence occurs. From figure 4.9 can be seen that the time of delay increase from 1 minute to 10 minutes also affects the average diameter of microparticles from 1.76um to 2.26um which is an increase of about 0.5um.

Coalescence can have a significant impact on particle size distribution, when particles coalesce, they merge together to form larger particles, which can lead to a shift in the size distribution of the particles. The extent of this shift depends on various factors such as the size of the particles, the rate of coalescence, and the conditions under which the coalescence occurs. From figure 4.9 can be seen that time of delay increase from 1 minutes to 10 minutes also affect the average diameter of microparticle from 1.76um to 2.26um which is increase about 0.5um.

Delay	Emulsion microparticles of PMMA-co-MAA (40xmagnification)	Graph for size distribution of emulsion of PMMA-co-MAA
1 minutes		

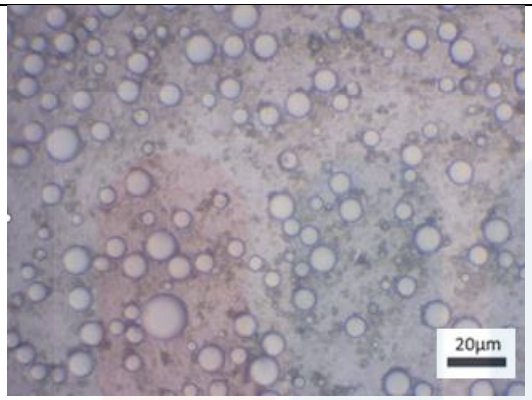
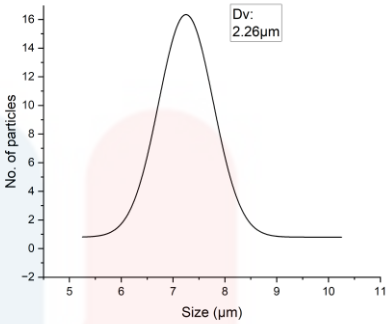
10 minutes		

Figure 4.10: Effect of time of delay during emulsification process to the average diameter of PMMA-co-MAA emulsion microparticles

CHAPTER 5

CONCLUSION AND RECOMMENDATION

5.1 Conclusion

In this study, different size and morphology of PMMA-co-MAA microparticles has been successfully obtained using two step solvent evaporation method assisted with ultrasonicator probe with different parameter, which are effect of water: oil ratio, effect of feeding rate, effect of amplitude of ultrasonicator probe and effect of delay.

The conclusion that has been made for this study has been divided into two parts, chemical parameter and physical parameter. Chemical parameters have showed that effect of water: oil ratio is one of suitable parameter to produce small uniform of microparticles, the smallest microparticle that can get through this parameter is 1.48um for water: oil ratio 7: 3. The applications that can be carried out are environmental remediation and biotechnology and diagnostics.

For the physical parameter is effect of feeding time, effect of amplitude of ultrasonicator probe and effect of delay. Among the best parameter to get smaller size of microparticles is effect of amplitude of ultrasonicator probe, when used 70% of amplitude where the pulse is 5 second run, and 5 second stop is the most optimum to prevent heat build-up during emulsification prosess. Hence smaller uniform size of microparticles can be obtained with is 1.48um.

In addition, the study about microparticles show in order to get small microparticle and successful emulsion need a good temperature control of temperature not more than 25C˚.

Lastly, PMMA-co-MAA are certificate as biocompatible material than can be safe for use. This presence potential requirement for biomaterial application use.

5.2 Recommendation

This study thoroughly supports the use of an ultrasonicator probe device to help the solvent evaporation process create a range of microparticle sizes. This approach is appropriate for researching how a parameter affects the size of the microparticles. But this method is not suitable for manufacturing in industrial manufacturing because the ultrasonicator probe creates an extremely sensitive atmosphere during the emulsification process. Additionally, a variety of parameters must be taken into account during the evaporation process in order to manage the rate of evaporation. This study's goal is to examine how a parameter affects the size of the microparticles. Consequently, use scanning electron microscope in order to acquire better images of the surface morphology of PMMA-co-MAA microparticle.

REFERENCES

Arefin, P., Habib, M. S., Ahmed, N., & Arefin, S. (2021). Microspheres and Microcapsules: A Review of Manufacturing Techniques for Pharmaceutical Industries. ResearchGate.

Cho, S., Choi, W. Y., Oh, S., Lee, C., Seo, Y., Kim, J., Song, C. H., Kim, G., Lee, S., Kang, D., & Lee, H. (2012). Enhancement of Lipid Extraction from Marine Microalga, Scenedesmus Associated with High-Pressure Homogenization Process. Journal of Biomedicine and Biotechnology, 2012, 1–6. https://doi.org/10.1155/2012/359432

Deka, N., Bera, A., Roy, D., & De, P. (2022). Methyl Methacrylate-Based Copolymers: Recent Developments in the Areas of Transparent and Stretchable Active Matrices. ACS Omega, 7(42), 36929–36944.

Experts, C. M. (2021). What is a microsphere? Definition and explanation. - Microspheres online. Microspheres Online.

Geri, M., Keshavarz, B., McKinley, G. H., & Bush, J. W. M. (2017). Thermal delay of drop coalescence. Journal of Fluid Mechanics, 833, R3.

Hoa, L. Q., Tai, N. T., Nguyen, L. V., & Chien, D. M. (2012). Preparation and characterisation of nanoparticles containing ketoprofen and acrylic polymers prepared by emulsion solvent evaporation method. Journal of Experimental Nanoscience, 7(2), 189–197.

Hosseini, S., Ibrahim, F., Djordjevic, I. B., & Koole, L. H. (2014). Polymethyl methacrylate-co-methacrylic acid coatings with controllable concentration of surface carboxyl groups: A novel approach in fabrication of polymeric platforms for potential bio-diagnostic devices. Applied Surface Science, 300, 43–50.

Ilhan, M., & Ilhan, M. (2024, January 17). What are the differences between microspheres and microcapsules? Oakwood Labs.

Jane. (2022, May 31). What Is Effect Of Molecular Weight On Polymer Properties? - On Secret Hunt. On Secret Hunt -.

Labrotovap. (2020, January 18). What is a Ultrasonic homogenizer (sonicators)？ - Lab Instrument Manufacturer. Lab Instrument Manufacturer.

Lengyel, M., Kállai-Szabó, N., Antal, V., Laki, A. J., & Antal, I. (2019). Microparticles, Microspheres, and Microcapsules for Advanced Drug Delivery. Scientia Pharmaceutica, 87(3), 20.

Polymers, A. (n.d.-a). Molecular Weight and The Effects on Polymer Properties | Amco Polymers. Amco Polymers.

Polymers, A. (n.d.-b). Molecular Weight and The Effects on Polymer Properties | Amco Polymers. Amco Polymers.

Rivas, C. J. M., Tarhini, M., Badri, W., Miladi, K., Greige-Gerges, H., Nazari, Q. A., Rodríguez, S., Román, R., Fessi, H., & Elaissari, A. (2017). Nanoprecipitation process: From encapsulation to drug delivery. International Journal of Pharmaceutics, 532(1), 66–81.

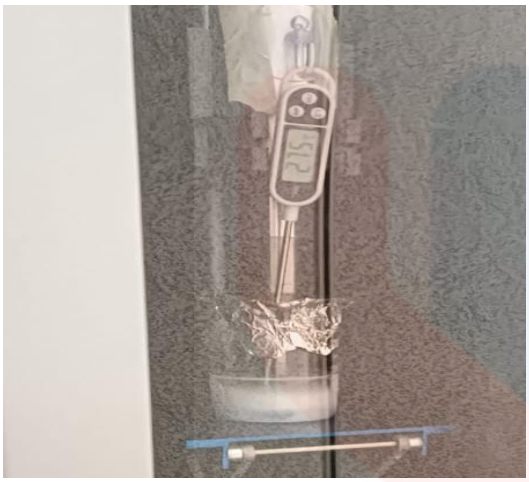
Salawi, A. (2022). Self-emulsifying drug delivery systems: a novel approach to deliver drugs. Drug Delivery, 29(1), 1811–1823.

Ultrasonics, H. (2023). Ultrasonic Homogenizers for Liquid Processing. Hielscher Ultrasonics.

Wischke, C., & Schwendeman, S. P. (2008). Principles of encapsulating hydrophobic drugs in PLA/PLGA microparticles. International Journal of Pharmaceutics, 364(2), 298–327.

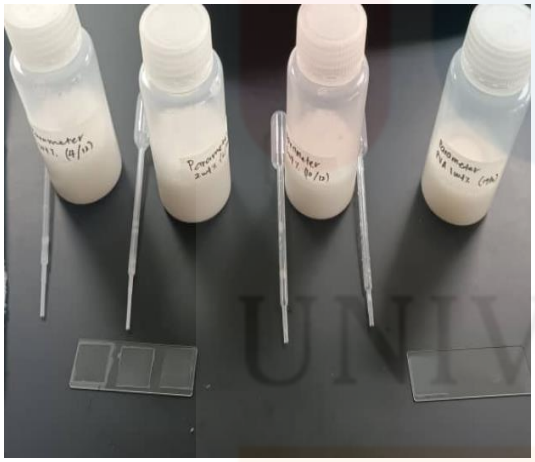
Yu, C., Yin, B., Zhang, W., Cheng, S., Zhang, X., & Zhuo, R. (2009). Composite microparticle drug delivery systems based on chitosan, alginate and pectin with improved pH-sensitive drug release property. Colloids and Surfaces B: Biointerfaces, 68(2), 245–249.

APPENDIX

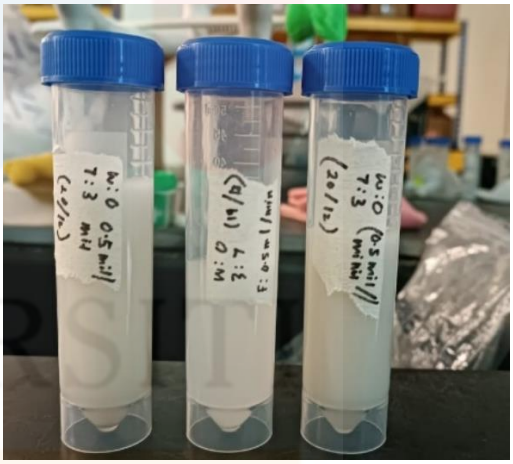


A.1: The emulsifying process by using ultrasonicator.

A.2: Solvent evaporation process using rotatory evaporation.



A.3: Preparation for viewing microscope



A.4: The finished emulsion