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*Louisiana State University and Agricultural and Mechanical College*

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# EFFECT OF PROCESS MIXING ON THE SIZE DISTRIBUTION AND MEAN DIAMETER OF THE THIOL-TRIACRYLATE MICROCAPSULES

A Thesis

Submitted to the Graduate Faculty of the  
Louisiana State University and  
Agricultural and Mechanical College  
in partial fulfillment of the  
requirements for the degree of  
Master of Science

in

The Gordon A. and Mary Cain Department of Chemical Engineering

by

Rubaiyet Abedin

B.S., Bangladesh University of Engineering and Technology, 2009

May 2014

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## **ABSTRACT**

An important limitation in the development of the microparticles is the difficulty to develop a precise size distribution. Microparticles have a wide spread applicability in different fields including medical, pharmaceutical, textile, cosmetics, pesticide, printing industry, etc. The large and growing impact of microencapsulation in different fields of technology has made this process important. Microparticle size is a primary determinant of control release mechanism and the reaction kinetics and also impacts the allowable routes of administration, The main objective of this research work is to evaluate the effect of the process mixing on the size and size distribution of the trithiol-triacrylate microparticles prepared via dispersion polymerization using the primary amine catalyzed addition of trithiol to triacrylate. The influence of several synthesis parameters such as, the stirring rate, oscillation frequency and amplitude, surfactant concentration in the aqueous phase on the size distribution of the microparticles has been investigated. A comparison between the reactor with three blades propeller and oscillatory reactor in terms of particle size distribution and energy dissipation per unit mass has been reported. A laboratory investigation has been performed to identify the most suitable reactor based on the desired size distribution of the microparticles. The experimental results indicate that oscillatory reactor is more suitable to achieve small particle size and narrow size distribution.



## **CHAPTER 1- INTRODUCTION**

Microencapsulation is an advanced approach used to immobilize, protect, isolate and control the rate of transfer of core materials, thereby improving the quality of the industrial commercial product. It can be used to extend the shelf life of the core component, preserving the properties which are commercially beneficial. Prolonged storage ability undermines the loss of degradation (Madene et al., 2006; Pena et al., 2012). These facts have helped to promote the microencapsulated particles in different process, and especially where the possibility to control the reaction kinetics exists. The size of the microparticles plays an important role in the process kinetics and release mechanism. Lack of the ability to predict and control the size distribution of the microparticles can be a problem leading to the inability to predict the chemical properties of the particles accurately and the extent of materials availability.

The aim of this research is to compare the ability of two different reactor types to produce microparticles. Microparticles will be produced by the method described by Bounds et al. Bounds et al. described a novel approach to prepare microparticles using trithiol and triacrylate by dispersion polymerization. In this process, a primary amine is used as the initiator and the produced microcapsules consist of a solid matrix enveloping pockets of core material. This process is different from a normal microencapsulation process where the final particle is a thin shell containing a liquid core. The chemistry used to prepare these microcapsules is a versatile in terms of synthesis flexibility. To vary the properties of the microcapsules a multitude of different monomers can be used. The reaction can be modified using different core material giving the improvement of desired characteristics. This type of microparticles can be used for simulated release or controlled release mechanisms depending on the core material used (Bounds et al., 2012). Traditionally, this type of macro and micro scale synthesis is done using a propeller

reactor. The primary objective here is to evaluate the performance of a piston driven reactor to achieve a narrow size distribution.

The first chapter of the thesis dissertation focuses on the background and motivation. The aim of this research work is to investigate the size and size distribution of the microparticles by manipulating different operational and design variables. To understand the importance and impact of the size distribution it is necessary to know about microencapsulation. Chapter 2 focuses on the microencapsulation process, application and different procedure and the impact of size distribution. In Chapter 3, the effect of process mixing is investigated. All the experimental work has been done by controlling process parameters and using different reactor types. The corresponding effects on the mean size and size distribution of the microparticles have been characterized in this chapter. Finally, the fourth chapter lists some prospective future work.

## **CHAPTER 2- LITERATURE REVIEW**

### **2.1 Microencapsulation**

Microencapsulation is the technique in which one material or mixture of materials is coated with a thin protective film or entrapped within a homogeneous or heterogeneous matrix, to provide a physical barrier between the core compound and the environment. This technique has been first employed to produce pressure-sensitive coatings for the manufacture of carbonless copying paper in 1955 (Green and Scheicher, 1955). Since then numerous research works have been going on for the development of microencapsulation products. During 1980 microencapsulation was examined by US National Aeronautics and Space Administration (NASA) as a novel approach to reduce the impact of extreme variations in temperature encountered by astronauts during their mission in space. Though it has not been adopted by the space program, the potential of microencapsulation was introduced to different fields (Nelson, 2002). Microencapsulation is now a well-established cost effective technology and accepted in many fields of science. It involves a number of processes to protect an active compound with a protective barrier that can be imparted under certain conditions such as shear stress, time, mechanical circumstances, osmotic pressure, reaction, and migration, pH change, temperature, enzymatic activities. The process not only to encapsulates the active material or ingredients, but also increases the shelf life of active materials, helps to handle the toxic material safely, helps to mask the distasteful flavors in food products, and often most importantly controls the release of core material, etc. The active material or ingredients is called the core material, internal phase or fill and the outer material used to encapsulate is referred to as the shell, wall, carrier or encapsulant. The core material may be a crystalline material, an emulsion, a suspension of solids, a suspension of smaller microparticles or a jagged absorbent particle. The shell may consist of

multiple layers depending on the nature of application. Generally the shell material has no reactivity with the core material; the shell material is used only to protect the core by locking it up in a membrane thereby creating a barrier from the exterior medium. The choice of external shell depends on a number of factors including the purpose of the shell, nature of the core material, the process of encapsulation, product objectives and application, requirement of the process, process economy, time effect, etc. A schematic illustration of microparticles has shown in Figure 2.1.

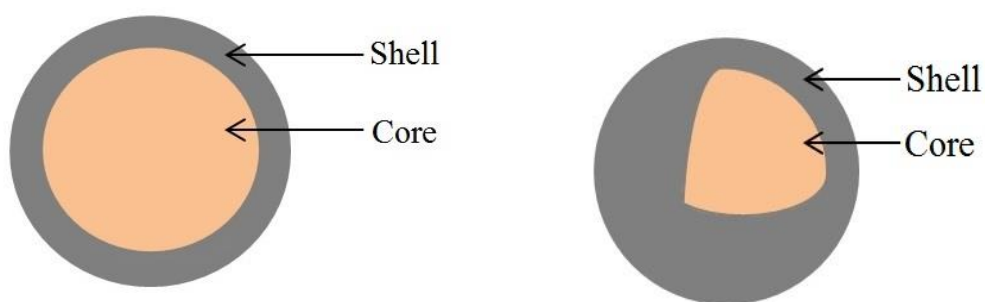


Figure 2.1 Schematic illustrations of microparticle

Depending on the application, technique used for encapsulation, core properties, the matrices of encapsulation can be of various shapes including film, sphere, irregular shape, various structures: porous or compact, various thicknesses: uniform or non-uniform and various physical structures: amorphous, crystalline, rubbery, glassy, etc. Some different shapes of microparticles have been illustrated in Figure 2.2.

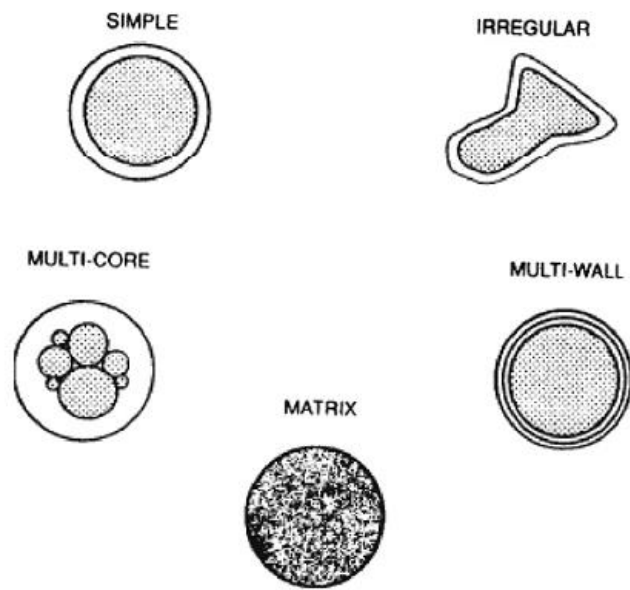


Figure 2.2 Different types of morphology of microparticles (Gharasallaoui et al., 2007)

## 2.2 Application of Microencapsulation

The simplicity and flexibility of microencapsulation has made it easily adaptable to many process. Collective application of microencapsulation include application in food industry, cosmetics, textiles, agriculture, medications or drug delivery system, printing industries- carbonless copy paper, pesticides, etc.

Encapsulation is widely used in food industry for applications such as protection from reactive environment (oxygen, water, acid, etc.), controlled or sustained release- both time controlled and temporal release, stabilization of the ingredients during processing, masking flavors , colors or odors, protecting components against nutritional loss, extension of the shelf life. Flavor and aroma are two sensitive and important components for food products which are difficult to control. By encapsulating these components it becomes possible to limit the loss during processing and storage, limit the degradation and control the quality of the products.

Vitamin, fats and oils, enzymes, minerals, colorants, aroma compounds are often encapsulated to maintain the quality. Carbohydrate, starch, protein, maltodextrin, gums are often used as shell materials (Madene et al., 2006). Since mid-1950 there have been increasing number of publications (scientific, non-scientific articles and patents) on microencapsulation techniques used in food industry (Gouin, 2004). Figure 2.3 illustrates the upward trend of microencapsulation publications in food processing industry.

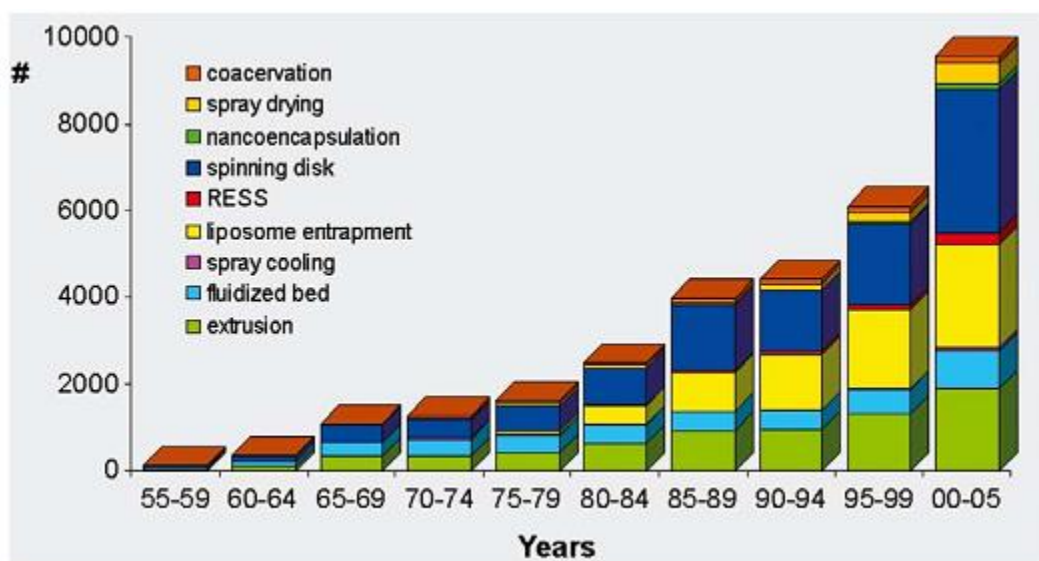


Figure 2.3 Trends in microencapsulation technology; Reference source: Chemical abstract (Gouin, 2004)

In the textile industry, microencapsulation has been used for imparting finishes and properties such as abrasion resistance, water repellent, leather aspect, improvement and durability of the aroma of the fabrics by using essential oil, perfume release etc. With the intention of ensuring a long-lasting fragrance, currently the perfume encapsulation technology is being used for the development of innovative textile products. Pena et al. has investigated the

process of encapsulating vanillin as a perfume component and promoting suitability for a long lasting release (Pena et al., 2012). Another study has demonstrated the encapsulation of flame retardant in a commercial coating for textile applications (Giraud et al., 2005).

Periodic direct application of pesticide in the form of powder, granules or concentrated emulsion can cause environmental contamination, which can affect terrestrial and aquatic ecosystems. The potential risk can be decreased by using the pesticides in the microencapsulated form. Alachlor, fonofos, pyrethrin, methyl parathion, diazinon, etc. insecticides are already being marketed as microcapsules. Rivas et al. has described the procedure of the encapsulation of pyrethroid into polyurea microparticles (Rivas et al., 2006). Encapsulated microparticles can be used to reduce environmental toxicity as well as the reduction of green contamination, extend activity, reduce evaporative losses and leaching, protect ecosystem from potential risk and environmental degradation and reduce the active pesticide levels in the environment. The presence of pharmaceutically active compound (PhAC) can be harmful to the ecosystem. Whelehan et al. has studied the recovery of seven PhAC from aqueous solution using liquid-core microparticles including the feasibility, kinetics and the efficiency of the process (Whelehan et al., 2010). Due to undesirable side effect involving toxicity and carcinogenicity, it is necessary to remove 2-*sec*-butyl-4,6-dinitrophenol (DNBP) from the environment. The process of the removal of DNBP from aqueous solution has been investigated by Wang et al. using encapsulated potassium ferrate (VI) ( $K_2FeO_4$ ) (Wang et al., 2009).

The potential impact of cell microencapsulation technologies is enormous from a therapeutic and economic perspective. This technology can be used in the treatment of numerous medical diseases including cancer, central nervous system diseases and endocrinological disorders. Long term production of therapeutic products from the encapsulated cells can be used

for the treatment of chronic diseases like Hyperparathyroidism, Parkinson's disease, Hemophilia, Diabetes mellitus, hepatic failure. (Murua et al., 2008). The controlled, continuous, delivery of therapeutic products by the immunoisolated cells is a cost effective method. Researchers believe that the potential of cell microencapsulation is enormous and it can make significant contributions to medicine over the next decade (Orive et al., 2004).

The controlled-release properties of microparticles are extensively used for many prescription and non-prescription medications, some of which can be taken orally. Microencapsulation can be used to obtain long acting injectable drug depot formulations and specific drug targeting options. Microparticles provide an alternative to multiple injections to obtain sustained release of the drug with a single administration. Herrero-Vanrell et al. reported the ongoing research of the biodegradable polymeric microparticles loaded with drugs for the delivery by intravitreal injection to treat diverse vitreoretinal diseases (Vanrell and Refojo, 2001). Abdelbary et al. studied the encapsulating process of glipizide, which is a second generation sulfonylurea that can acutely lower the blood sugar level in human by stimulating the release of insulin from the pancreas, within certain hydrophilic polymer to control the release of this highly water insoluble drug (Abdelbary et al., 2012). Tu et al. described the process of encapsulating hydroxybenzoic acid (p-HBA) and lysozyme within a bioerodible polymer using a carbon dioxide antisolvent (Tu et al., 2002). Another study reported the development of the encapsulation process of antigens and their release from polymeric systems in a controlled and timely manner (Sanchez et al., 1996). Researchers are hopeful that in near future the encapsulation technique might be developed as one of the important part of the treatment of various neurological degenerative diseases (Miyoshi et al., 1996). All this studies clearly indicate the prospective advances in the field of medicine and pharmacy.



The manufacture of fermented dairy products, such as cheese, yogurt, frozen dairy desserts, cultured cream, mayonnaise, and biomass production has been facilitated by the encapsulation of micro-organisms. As a matter of fact, micro-organisms are protected from bacteriophage and harsh environments, which elongates their shelf life. Kailasapathy illustrated the encapsulation process of probiotic bacteria, potential application in the food industry and dairy technology, and prospective application in the health food industry for direct consumption and for external application (Kailasapathy, 2002). Other study also verifies that the microencapsulation of various bacterial cultures including probiotics facilitates the manufacture of fermented dairy products by keeping constant characteristics of the bacteria, extending the storage life and enhancing the ease of application (Krasarkoopt et al., 2003).

Using microcapsules as biocatalyst or catalyst in different medium and process, the viability of the products can be enhanced and targeted delivery can be ensured. From environmental and economic viewpoint, encapsulated heterogeneous biocatalysts are more desirable than homogeneous catalyst for a more sustainable industrial growth. Buonomenna et al. has reported the catalytic activity of a novel heterogeneous catalyst polyvinylidene fluoride (PVDF) microparticle for the selective oxidation of benzyl alcohol (BzOH) to benzaldehyde (BzH) (Buonomenna et al., 2008). Study indicates that, the use of encapsulated microbial cells and enzymes as biocatalyst plays a significant role in increasing the efficiency of the bioreactor (Park and Chang, 2000). Grenn et al. has carried out the process of encapsulation of yeast cells and their growing importance as a biocatalyst in the production of food ingredients, pharmaceuticals and fine chemicals (Green et al., 1996).

Advanced ongoing research includes the encapsulation of DNA, hormone, etc. Walter et al. has reported a promising method of encapsulation to prepare delivery systems for DNA

vaccination and represented the design of DNA vaccination delivery systems for the targeting of professional antigen presenting cells as an interesting approach to fight viral infections and in cancer therapy (Walter et al., 1999). Controlled release of therapeutic proteins such as growth hormones, growth factors, cytokines for a desired period of time can be accomplished by encapsulation. Kim et al. has described the process of encapsulating recombinant human growth hormone (rhGH) within poly(D,L-lactic-co-glycolic acid) microparticles (Kim and Park, 1999). Donal et al. has demonstrated the encapsulation process of steroids in poly(lactide-co-glycolide) microparticles to incorporate long-acting drug delivery system (Cowsar et al., 1985).

### **2.3 Different Process of Microencapsulation**

Microencapsulation is not only used for controlled release or target delivery, it also used to add values to the product. Gouin et al., Wieland et al. has described a number of techniques that are used to microencapsulate materials in a number of different industries including spray drying, spray chilling/cooling, coacervation, fluidized bed coating process, solvent evaporation, centrifugal extrusion, rotational suspension separation, interfacial polymerization (Gouin, 2004; Wieland et al., 2002).

Spray drying is the most common, well-established, straight forward, flexible and economical method of encapsulation. In this process, core or wall material is atomized through a nozzle or spinning wheel in the presence of co-current or counter-current hot air flow. Schematic illustration of microencapsulation process by spray drying has been shown in Figure 2.4.

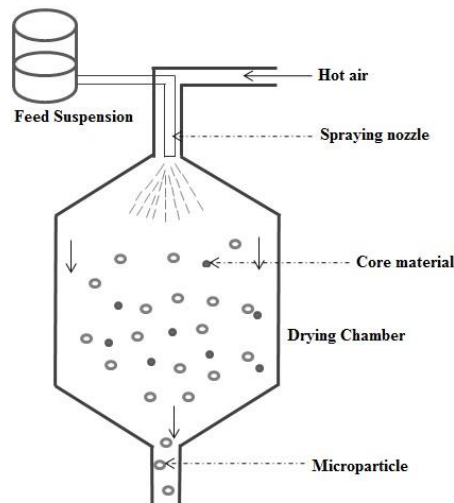


Figure 2.4 Schematic illustration of spray drying process

Food ingredients such as flavors, lipids and carotenoids are encapsulated mostly using this process, and this technology is now becoming available to satisfy the increasingly specialized necessity of the market. Gharsallaoui et al. has represented an overview of the application of spray drying in microencapsulation of food ingredients using different shell materials, the technical and operational conditions for the spray drying process (Gharasallaoui et al., 2007). Teixeira et al. has used this process to encapsulate short chain fatty acid within the shell produced by gum Arabic and maltodextrin mixture (Teixeira et al., 2004). Spray cooling or spray chilling is similar to this process except for the facts that the core material is dispersed in a liquefied coating or wall material and cooled or chilled air is used instead of hot air. This technology is used to encapsulate a number of organic and inorganic salts, enzymes, flavors, and other ingredients to improve heat stability, delay release in wet environments, etc. properties and is often regarded as one of the least expensive encapsulation technology (Gouin, 2004).

Coacervation is often regarded as the original, unique and rather expensive encapsulation technology. The theory behind it is the phase separation of one or many hydrocolloids from the initial solution, and the subsequent deposition of the newly formed coacervate phase around the active ingredient suspended or emulsified in the same medium. Generally different types of oils, vitamin are encapsulated using this method (Gouin, 2004). Arshady has presented a methodological survey of the coacervation technique used to manufacture the microparticles and has exemplified the effect of manufacturing parameters on microparticle characteristics (Arshady, 1989). Figure 2.5 illustrates the schematic representation of coacervation process.

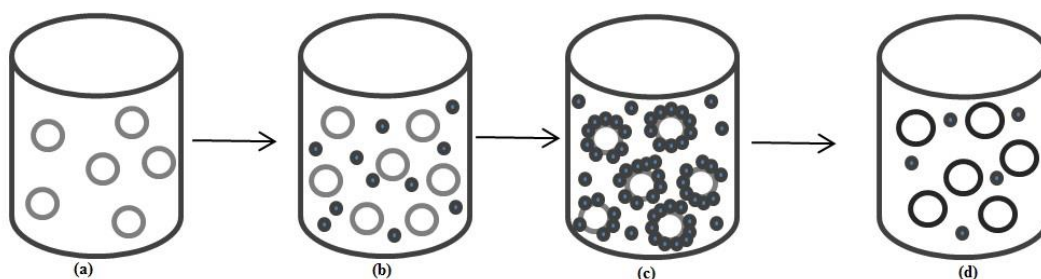


Figure 2.5 Schematic representation of the coacervation process; (a) Dispersion of core material in shell polymer solution, (b) Coacervate separation from solution, (c) Coating of core material by coacervate droplet, (d) Coalescence of coacervate to form continuous shell around the core.

One of the few efficient and advanced technologies to apply an identical layer of shell material onto solid particles is fluidized bed technology (schematic illustration -Figure 2.6), which is also competent for controlled release applications. This process is becoming a promising technique of encapsulation for large scale production. In this process shell material is sprayed onto the individual solid core particles in liquid form and the coated particles are either dried by solvent evaporation or cooling in a zone where they are being cycled again and again

unless until they attain a certain coating thickness. The main advantage of this technology is the handling capability of a wide range of coating formulations such as polysaccharides, proteins, emulsifiers, fats, complex formulations, enteric coatings, powder coatings, and yeast cell extract (Benita, 1996). Krober et al. described a novel fluidized bed coating process to encapsulate fine and heat sensitive solid particles using super critical carbon dioxide (Krober and Teipel, 2005). Santos et al., Perrut et al have demonstrated the process of encapsulation based on supercritical fluid (SCF) technology (Santos et al, 2002; Perrut and Clavier, 2003).

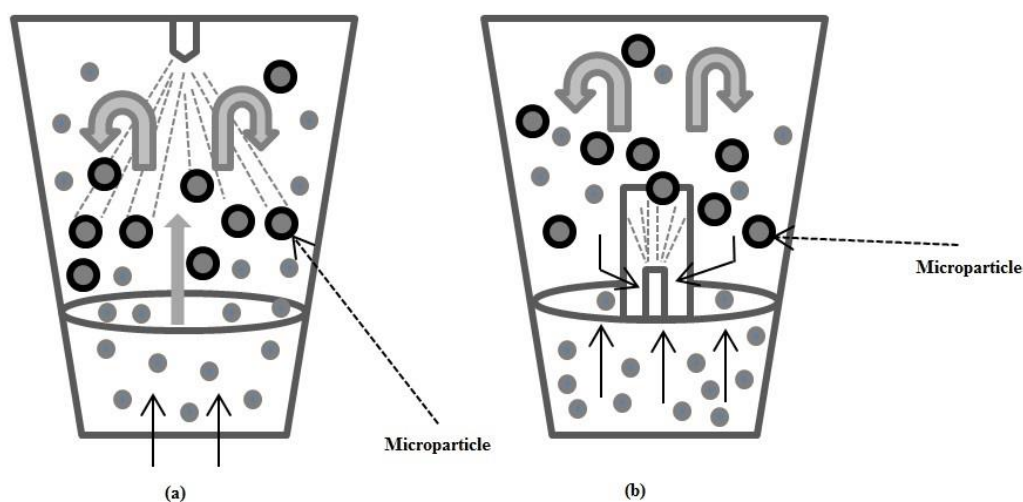


Figure 2.6 Schematic representation of fluidized bed process; (a) Top spray, (b) Bottom spray

The technique of microencapsulation by the solvent evaporation method is widely used in pharmaceutical industries. In the solvent evaporation process the core material is dispersed or dissolved in the polymeric water immiscible solvent, and this dispersed solution is emulsified in an aqueous continuous phase to form discrete droplets and later on the water is evaporated leaving the hardened microparticles. Generally water insoluble polymers are used as

encapsulation matrix and different types of drugs including steroids, narcotic agents, fertility control agents, anti-cancer drugs, local anesthetics, insulin, vaccine, cisplatin, lidocaine, naltrexone are encapsulated using solvent evaporation process. Patrick et al. has summarized the advances in the solvent evaporation method to produce biodegradable poly(lactic acid) (PLA) and poly(lactic-co-glycolic acid) (PLGA) microparticles (O'Donnel and McGinity, 1997). Li et al. has reviewed the process of encapsulation by solvent evaporation and focused on the physical properties of the material and operating condition, different aspects of microparticles; hence studied the numerical model based on the solvent evaporation technique (Li et al, 2008).

Another type of encapsulation, which is highly suitable because of its simplicity, promptness, high loading capacity and hefty production scale, is interfacial polymerization. In this process microparticle shells are formed by polymerization of reactive monomers. A new technique for encapsulation of an insect growth regulator pyriproxyfen using interfacial polymerization has been reported by Tsuda et al. and the produced microparticles exhibit an intriguing property of bursting spontaneously (Tsuda et al, 2012). Hirech et al. has described the procedure to obtain insecticide microparticles by interfacial polymerization, which is processed in a stirred-batch reactor (Hirech et al., 2003). In situ polymerization is analogous to interfacial polymerization except the fact that no reactive agents are added to the core material. This kind of polymerization is used to produce small microparticles loaded with carbonless paper inks or perfume for scented strips and the polymerization occurs in the continuous phase and microcapsule shell is formed at the interface of dispersed core material and continuous phase (Benita, 1996).

Extrusion is exclusively used to encapsulate volatile and unstable flavors. During this process the dispersion of the core material in a molten mass is forced through a die into a

dehydrating liquid, and it hardens the coating to trap the core material. The schematic diagram of extrusion process has been presented in Figure 2.7. The main disadvantage of this process is the formation of large particles and limited range of shell material (Gouin, 2004).

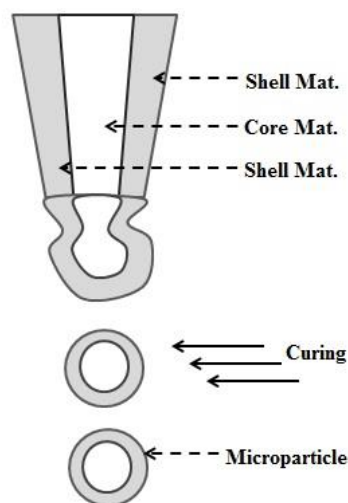


Figure 2.7 Schematic diagram of extrusion process

Centrifugal extrusion is the process in which a spinning two-fluid nozzle is used to produce two-fluid (mutually immiscible liquid-core and the shell material) column or rod that breaks up into a stream of spherical droplets spontaneously after it emerges from the nozzle (Benita, 1996). Rotational suspension separation is claimed to be a cost effective, fast, high volume method of encapsulating materials in which the core material is suspended into the shell material and this mixture is introduced onto a conical or bowl shaped rotating disk. The encapsulated particles are whirled off the disk and then dried or chilled (Benita, 1996). There are several other methods used to synthesize microparticles depending on the core and shell

materials and the morphology of the produced capsules, such as phase separation (Atkin et al., 2004), suspension polymerization (Sanchez-Silva et al., 2010).

Micron sized mono-disperse microparticles are used in a number of variety applications. Dispersion polymerization is an ideal method for producing micron sized monodisperse polymer particles in a single batch process. This kind of polymerization involves a homogeneous solution of the monomer with initiator and dispersant, in which sterically stabilized particles are formed by the precipitation of resulting polymer. A schematic illustration of dispersion polymerization is presented in Figure 2.8. Different kinds of dispersion polymerizations using different polymer dispersant and the mechanism of dispersion polymerization has been demonstrated by Kawaguchi et al. (Kawaguchi and Ito, 2005).

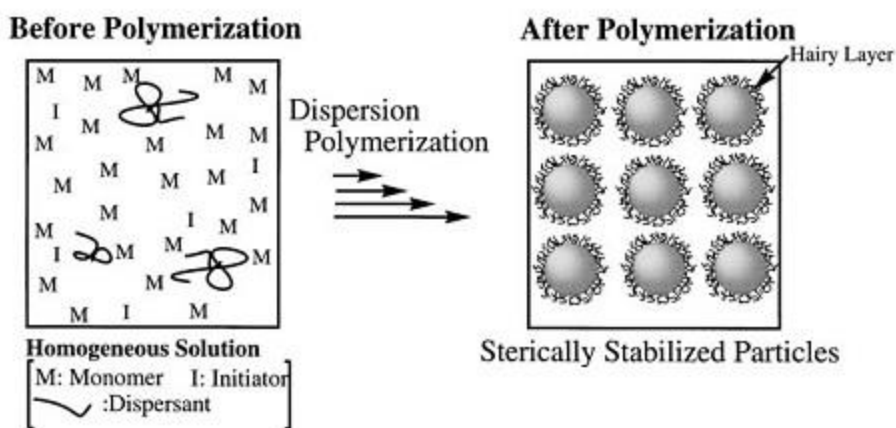


Figure 2.8 Schematic illustrations of dispersion polymerization (Kawaguchi and Ito, 2005)

## 2.4 Control of the Microparticle Size

Microcapsules can entrap different chemicals, food ingredients, flavors, aroma, drug, yeast, enzymes, live cells, insulin, vitamin, minerals, ink (Madene et al., 2006). The size of the



commercially produced microparticles vary between 3 and 800  $\mu\text{m}$  and contain about 10-90 wt. percent core (Benita, 1996). Size and size distribution of the microparticles has a great impact on the process mechanism, reaction kinetics, allowable routes of administration, release rate of the encapsulated core materials. The change in the process parameter of the microparticles can influence the properties and the performance of microparticles such as, mechanical strength, ease of filtration, friability, etc. (Nesterova, 2012). Microparticle applications are basically administrated by the size, shape and morphologies of the microparticles. Smaller microparticles may exhibit poor encapsulation efficiency, undesirable release of the core material or migration from the site of injection. Larger microparticles may also exhibit poor encapsulation efficiency due to elongated release time and undesired sizes. Some critical applications require microparticles of specific size. For such applications, poly-disperse microparticles must be filtered, sieved or separated to produce microparticles of a desired range using different techniques.

Particle size has a tremendous effect on the release rate and the drug delivery system. The particle size distribution containing anticancer drugs ranged from 1 to 30  $\mu\text{m}$  and by mixing microparticles of smaller size with larger size a release profile with intermediate release rate can be attained. Thus controlled release can be moderated by appropriate mixing of the microparticles of different sizes to ensemble the requirements of cancer chemotherapy (Narayani and Rao, 1996). In the drug delivery system, relative drug release rate decreases with the increasing size of microparticles regardless of the type of drug. The composition, micro particle size and the manufacturing process can strongly affect the system properties, kinetics and the drug release mechanism (Siepmann et al., 2004). Cell encapsulation allows the transplantation of non-human cells that could be considered as an alternative to the limited supply of donor tissue, and it allows

the delivery of the product for a longer period of time as cells release the products continuously. For this type of application, the desired microparticle size is within the range 100-500  $\mu\text{m}$ , and these small microparticles allow their implantation in close contact to the blood stream, which is beneficial in some specific application of cell encapsulation (Murua et al., 2008). Microencapsulation of live BCG organism for the targeted delivery to the lung is also dependent on the particle size. Desired size of microparticles for the delivery of BCG vaccine to the lung is 5-15  $\mu\text{m}$  (for injecting the particles intravenously targeted to the lung as a result of entrapment within the lung capillaries) or 1-5  $\mu\text{m}$  (for delivery by inhalation) (Kwok et al., 1991). Study shows that for immobilizing living bacterial cells, the capsule size is a crucial factor and for industrial application design and development of equipment to generate precise and uniform microparticles are required (Kailasapathy, 2002).

Control of microparticle size and size distribution is also important implications in other applications too. For example, metal ion extraction application by encapsulating an extracting agent. Using small microparticles (for copper ion mean dia. 10  $\mu\text{m}$ ) can give a large interfacial area, which will enhance the extraction kinetics and mechanical resistance for more intensive use (Lagucir et al., 2002). The acceptable size for the microparticles filled with reactive healing agents into coating matrix used for a heavy duty anticorrosive coating layer is 100-200  $\mu\text{m}$ . Microparticles smaller than that cannot contain the required healing agent, larger than that can moderate the mechanical and visual properties of the coatings (Nesterova et al., 2012).

A major issue in fabricating the microparticle products is controlling the size distribution and for controlled release drug delivery technologies, a long sought goal is the ability to control the release rate of encapsulated compounds. Microparticle size plays an important role in the release kinetics. Whelehan et al. has emphasised the effect of microparticle size and membrane

thickness on the extraction rate of the liquid core (Whelehan et al., 2010). Microparticle size and size distribution often can be controlled poorly with standard deviations equal to 25-50% (Berkland et al., 2001). The process selected for microencapsulation depends on the desired size of the encapsulated products and the physiochemical properties of both shell and core materials. But the size of the microparticles also depends on the process of synthesis and reactant used.

In recent years there have been several reports of the fabrication of microcapsules with precise size distribution using several different approaches. Kwok et al. has described a novel method to produce microparticles of size range 5-15  $\mu\text{m}$  by air atomization technique. In this technique; liquid and pressurized air is fed to the atomizer forcing tiny liquid droplets out through the orifice of the nozzle, and the process is then followed by the centrifugation at a high rotational speed. The concept behind using the turbotak is to produce droplets within the desired size range, so that a narrow size distribution can be achieved (Kwok et al., 1991). Controlling the size of emulsion droplets and emulsification time, dynamic effect on the size distribution of microparticles can be obtained. Bahl et al. has demonstrated that decreases in the microparticles size as a function of emulsification time, mostly caused by the fragmentation of emulsion droplet upon stirring, is accompanied by the increases in the total number of microparticles and their surface area (Bahl and Sah, 2000). Several studies have indicated that fabricating different microfluidics continuous synthesis of microcapsules of desired size distribution can be accomplished. Using microfluidics devices for microencapsulation is a unique approach to attain fast and continuous production of polymer particles and microparticles with various shapes ranging from 20 to 200  $\mu\text{m}$  (Nie et al., 2005). Martin-Banderas et al. has described a versatile technology of encapsulation using flow focusing atomizer, which is another kind of microfluidic device which produces microparticles of controlled size and specific morphology. Flow focusing

technology is useful to produce small particles with different fluid combinations and the particle size is determined by the nozzle dimension (Martin-Banderas et al., 2005). Cho et al. has shown the procedure to prepare highly mono-disperse polymer/liquid crystal microparticles by solute co-diffusion method. In this method, a liquid crystal is dissolved in a solvent into the pre-existing mono-sized crosslinked polymer particles in the form of a fine emulsion. Polymer microparticles loading a single liquid crystal domain are obtained when the solvent is evaporated (Cho et al., 2002). Kontturi et al. has developed a laboratory scale simple, inexpensive and flexible device that can produce uniform small sized ( $< 300\ \mu\text{m}$ ) cell microparticles (Kontturi et al., 2011).

A number of studies show that microparticle size is also affected by different process parameters such as, emulsifier concentration, stirring rate, device parameter ratio, different phase volume, etc. Poncelet et al. has studied the impact of using different type of impellers, rotational speed, and emulsifier concentration on the mean diameter of hexanemethylene sebacamide microparticles and concluded that the selection of appropriate impeller design can affect the size distribution of the microparticles (Smet et al., 1990). Valot et al. has also reported the effect of different process parameters such as surfactant concentration, core material quantity, influence of the solvent used, volume of the different phases, stirring rate on the properties, especially the size and the size distribution of biocompatible Ibuprofen-loaded microparticles (Valot et al., 2009). The effect of process temperature and concentration of ethyl gellate on the size and structure of monodisperse poly(N-isopropylarylamide) has been represented by Mou et al. (Mou et al., 2012). Liu et al. has described the procedure of preparing uniform-sized biodegradable PLA/ PLGA microparticles loaded with recombinant human insulin (rhI) by combining a Shirasu Porous Glass (SPG) membrane emulsification technique and a double emulsion evaporation method (Liu et al., 2005). Poly( monomethoxypoly ethylene glycol-co-D,L-lactide) (PELA)

microparticles with narrow size distribution and smooth morphology can be prepared by combining premix membrane emulsification technique and double emulsion solvent extraction method (Wei et al., 2011).

## 2.5 Primary-Amine Catalyzed Thiol Acrylate Reaction Mechanism

Thiol Acrylate chemistry possesses some exceptionally useful properties which can be utilized in different fields. Bounds et al. has illustrated one reaction mechanism that can occur with thiols and acrylates (Bounds et al., 2012). The four step primary-amine catalyzed thiol acrylate reaction involves one pre-initiation, one initiation, and two propagation steps. The involvement of two propagation steps leads the reaction to be known as step growth polymerization. The reaction proceeds comprising the nucleophilic addition of the primary octylamine catalyst to the electron deficient ene. This step is known as pre-initiation step (Figure 2.9). The resulting carbanion from the pre-initiation step abstracts an acidic thiol proton and forms a thiolate anion, which is known as initiation of an anionic step-growth polymerization. Once initiated, unlike the free-radical thiol-ene mechanism, termination is not facilitated by the combination of two growing chains. The reaction is represented in Figure 2.10.

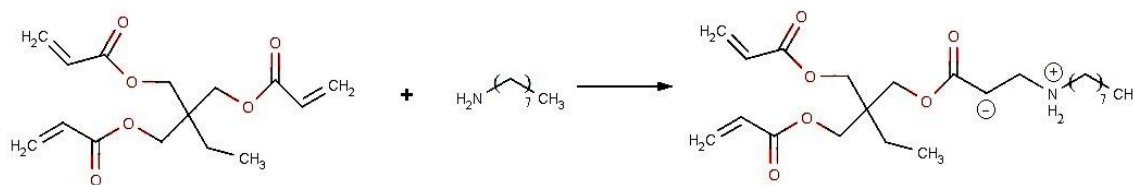


Figure 2.9 Reaction mechanism, Step 1: Amine Nucleophile Pre-initiation

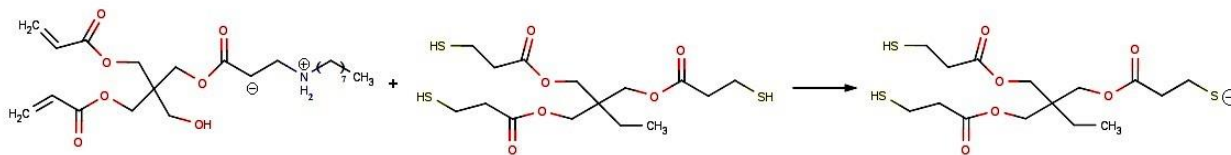


Figure 2.10 Reaction mechanism, Step 2: Initiation

The initiation step is then followed by two separate propagation steps. The first propagation (Figure 2.11) step involves the Michael addition of the deprotonated thiol anion to the electron-deficient ene group. Then a hydrogen transfer occurs between another thiol and the newly formed carbon anion.

This second propagation step (Figure 2.12) results in a chain transfer and another deprotonated thiol that will be activated for another Michael addition. This mechanism is basically a chain growth mechanism, and the second propagation step can be compared to a continuously sequential chain transfer step.

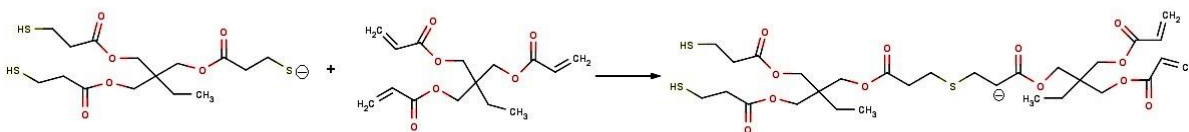


Figure 2.11 Reaction mechanism, Step 3: Propagation 1

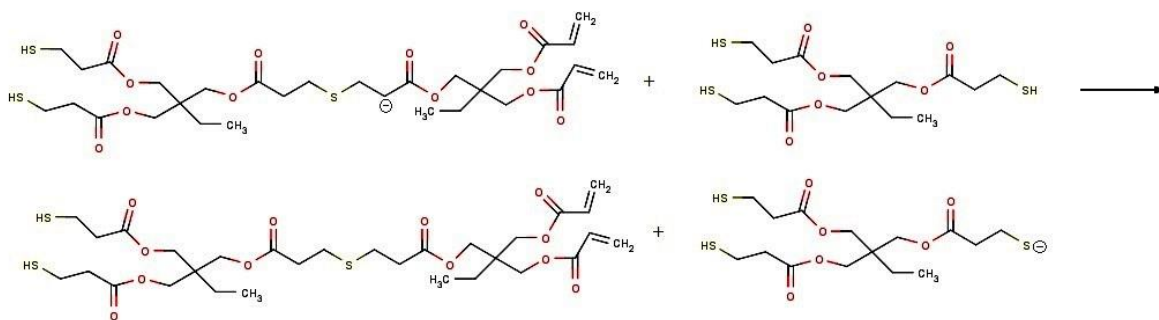


Figure 2.12 Reaction mechanism, Step 4: Propagation 2

This reaction is so fast that it needs very little time to reach high conversion, and this makes this process efficient and useful for many applications.

## CHAPTER 3- EFFECT OF PROCESS MIXING ON MICROPARTICLES

### 3.1 Introduction

Encapsulation is the technique in which a substance is coated with or entrapped within another material or system. The transfer of this substance can affect the surroundings (Madene et al., 2006). Different approaches are available in the literature for the preparation of microcapsules including spray drying, interfacial polymerization, in situ polymerization, fluidized bed coating, Centrifugal extrusion. Different polymer shell materials are available such as gelatin (Ugwoke et al., 1997), polyurethane (Tsuda et al., 2012), poly(tetrahydrofuran) (Atkin et al., 2004), poly(lactic acid), poly(N-isopropylarylamide) (Mou et al., 2012). Choice of the synthesis method and wall materials generally depends on the core material and the application. Some methods necessitate specific conditions including definite temperature rise, pressure, non-ambient conditions, lengthy reaction time, and multitude of components. Depending on the core material microcapsules can be used for either a stimulated release or controlled release. Bounds et al. studied the mechanism of microencapsulation using different core materials including dimethyl-para-toluidine (DMpT),  $\text{BF}_3$ -amine complex, Carbon nanotube, and  $\text{BCl}_3$ -amine complex. Rheology testing and Instron testing of the microparticles has been conducted to explore the rheological properties of the microparticles containing different core (Bounds et al., 2012). The trithiol-triacrylate method of encapsulation explored here has multiple advantages over other microencapsulation processes. These microparticles can be prepared at room temperature and at ambient pressure with a small number of components within one hour. The chemicals are reasonably safe to work with and inexpensive. Due to simplicity this process of encapsulation has been chosen for this research. This microencapsulation process can be described using the following flow diagram (Figure 3.1):



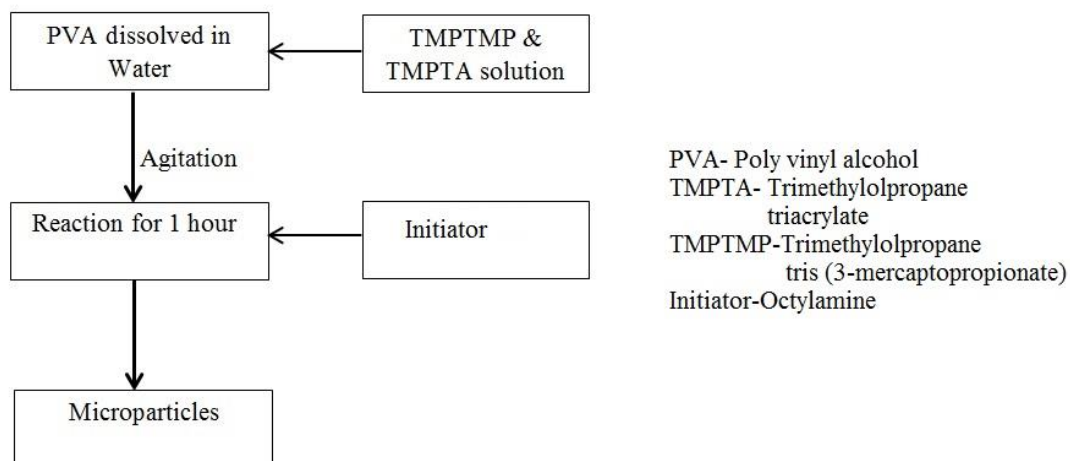


Figure 3.1 Flow diagram of the microencapsulation process

The aim of this research is the fabrication of this microparticle using trithiol and triacrylate and exploration of methods or reactor types to control microparticle size. Two different types of reactor (traditional stirred and piston driven) have been used to evaluate the effectiveness of the microencapsulation process and the size distribution of the microparticles. The synthesis parameters investigated are stirrer rate and surfactant concentration for the reactor with a three-blade propeller; and oscillation amplitude and frequency for the piston/oscillatory reactor.

### 3.2 Experimental

This section provides brief description of the experimental procedure used for the synthesis of the microparticles and concise report on the apparatus and the method used. The experimental procedure is basically a modified interfacial polymerization. Here an organic solution is dispersed in an immiscible aqueous solution, and polymerization occurs by means of a molecule containing a hydrophilic amino head and a hydrophobic hydrocarbon tail. An

overview of the reaction mechanism was given in Section 2.3. Microparticles prepared for investigation contain no core material.

### 3.2.1 Materials Evaluation

The materials used for this process are poly vinyl alcohol (PVA), trimethylolpropane triacrylate (TMPTA), trimethylolpropane tris (3-mercaptopropionate) (TMPTMP), and octylamine. Poly vinyl alcohol is used as surfactant and octylamine is used as initiator. Poly (vinyl alcohol) 87-89% hydrolyzed, trimethylolpropane triacrylate technical grade, trimethylolpropane tris (3-mercaptopropionate), and octylamine 99% were obtained from Sigma-Aldrich. All materials are used without further purification. Chemical structures are illustrated in Figure 3.2.

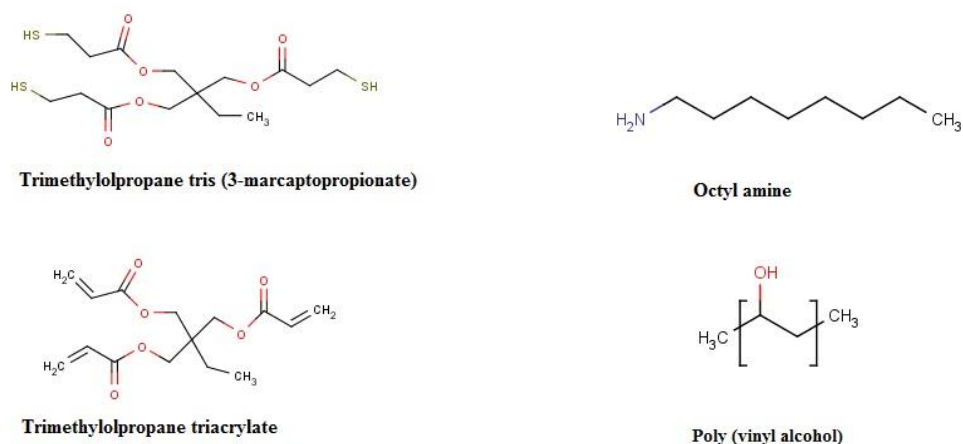


Figure 3.2 Chemical structure of the materials used for microparticle synthesis

### 3.2.2 Microparticle Preparation Method

The process of microencapsulation consists of the dispersion of a solution containing a core material dissolved in a stoichiometrically equivalent solution of the monomers. As this research work deals with the microparticles containing no core material, only the dispersion solution of stoichiometrically equivalent monomers has been prepared. We combine 15.94 g of TMPTMP and 11.85 g of TMPTA. The solution is then emulsified in 500 ml aqueous solution containing 1.28% PVA. For the emulsification, we use various amount and sources of energy in order to obtain a desired size of the microparticles. PVA is the surfactant to stabilize the system. In this research work two reactor types were evaluated. The first reactor is equipped with a three-bladed propeller. The second one is an oscillatory system in which a piston is used to supply the required shear force. The mixture is agitated or oscillated for 1 hour and 15 min at a defined rpm unless until the desired droplet size is achieved. Once the droplet size is satisfactory, approximately 3% by volume of octylamine is added to the mixture to initiate the polymerization. The complete reaction time is 1 hour 30 min. The whole encapsulation process is carried on at room temperature and ambient pressure. The produced microparticles are collected by filtering. Then they are dried for 12 hours in ambient air. Depending on the contained core material, solvents may be used to wash the excess core material from the exterior of the shell prior to the incorporation into a given system. This research work explores microparticles without any core material, and here the exterior of the microparticles are washed using distilled water.

### 3.2.3 Apparatus

The objective of this study is to evaluate the size of the microparticles using two different types of reactor: first a reactor with a three-blade propeller and second an oscillatory piston driven reactor. The first reactor consists of an IKA RW 20 DS1 digital overhead stirrer, which is equipped with a three blade propeller with a diameter 5.4 cm. A schematic of this reactor is illustrated in Figure 3.3.

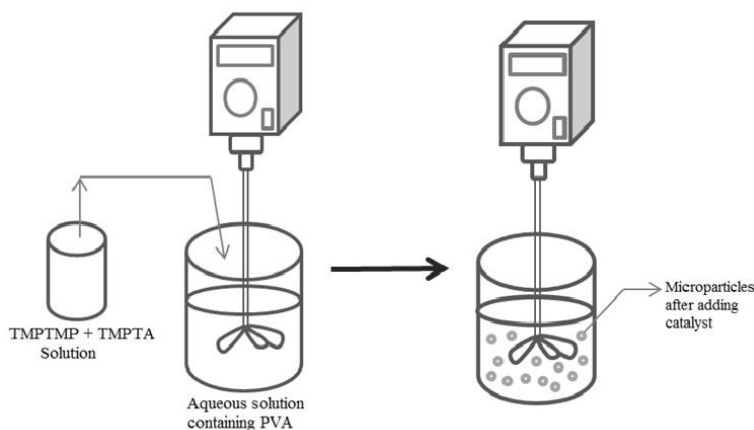


Figure 3.3 Diagram of agitation reactor

The oscillatory reactor is shown in Figure 3.4. The reactor consists of a stainless steel piston 10 cm diameter. The piston pushes against the bottom of the reactor which is a flexible rubber sheet. The rubber sheet seals the bottom of the reactor. The piston and the rubber sheet are flush with the reactor side walls leaving no dead volume, and it is driven by an electrical motor and a gear box. The oscillation frequencies can be controlled within the range of 1 to 25 Hz. By adjusting the eccentric positions of the shaft linking the piston and the drive unit, oscillation amplitude can be altered from 1 to 20 mm.

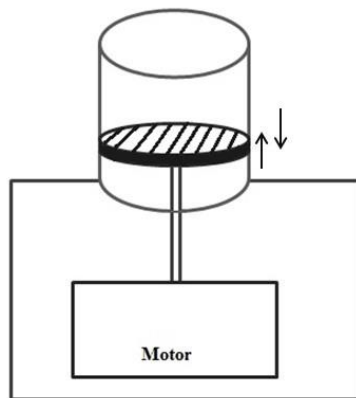


Figure 3.4 Diagram of oscillatory reactor

### 3.2.4 Characterization of Microparticles

The procedures used to determine the shape, size and the surface morphology of the microparticles are described in this section.

#### 3.2.4.1 Scanning Electron Microscopy

Microparticle surface features and diameters are determined using a JSM-6610LV Scanning Electron Microscope. The microparticles are sprinkled on metal stubs with double sided conductive adhesive tape and dried overnight. A thin platinum layer of approximately 15 nm thickness is used to coat the microparticles; an EMS 550x Sputter Coater is used.

#### 3.2.4.2 Size and Size Distribution

Microparticle size and size distribution are important factors for industrial application. In this work microparticle size was determined using a phase contrast Nikon ECLIPSE 50i microscope equipped with a Nikon Digital Sight DS-Fi1 camera. Small samples of the produced microparticles and liquid were spread over a glass coverslip immediately following the synthesis

and allowed to dry for 12 hours. This sample was then observed under the microscope with a magnification less than or equal to 10x. NIS-element BR 3.0 software determined particle size. Approximately 3000 particles were analyzed in each sample to determine mean particle diameter and size distribution. The variation in size distribution can be expressed in terms of the particle volume fraction. Particle volume fraction may be defined as,

$$Volume\ Fraction = \frac{n_i d_i^3}{\sum_{i=1}^n n_i d_i^3} \quad (1)$$

Here,  $d_i$  is the  $i$ -th particle diameter;  $n_i$  is the number of the particle with  $d_i$  diameter and  $n$  is the total number of the particles counted.

### 3.2.4.3 Power Input

Power consumption is the mechanical energy transferred from the impeller or piston to the fluid. The power input causes fluid motion, which can be used to correlate mixing and rates of mass transfer. Impeller power consumption ( $P$ ) is a function of impeller speed, diameter, location and design, reactor size and geometry, baffle design, etc. (Oldshue, 1983). To calculate the power consumption, correlations have been established primarily through extensive experimental work. Power consumption,  $P$  can be given by (Tatterson, 1991),

$$P = N_p \rho N^3 D^5 \quad (2)$$

Here,  $N_p$  is dimensionless power number, which relates the effect of geometry and flow regime to the power consumption.  $\rho$  is the density of the fluid.  $N$  is the impeller speed and  $D$  is the impeller diameter. The power number can be calculated using the associated Reynolds number of the fluid. Power consumption for the reactor with the three-blade propeller can be calculated. Power consumption per unit mass of liquid in the reactor with a vibrating piston can be expressed as (Knopf et al., 2006),

$$P_m = \frac{A^2 \omega^3}{2} \quad (3)$$

Here,  $P_m$  is power consumption per unit mass,  $A$  is the amplitude for the solid piston (constant) in mm, and  $\omega$  is the frequency of oscillation in rad/s.

### 3.3 Result and Discussion

Synthesis of the microparticles has been performed following the procedure developed by Christopher et al. (Bounds et al., 2012). Two different reactor types were evaluated. In this section, results of the studies will be presented in terms of the size of the microparticles.

#### 3.3.1 Microcapsules Characterization: Morphology and Size

The spherical shape of the microparticles has been observed using SEM microphotography. The SEM images show that the external walls of the microparticles are smooth. The images of the microparticles at three different rotational speeds (1000 rpm, 1700 rpm and 2000 rpm) are presented at the same magnification. Figure 3.5 shows the SEM images at x200 magnification and more small particles are seen to exist at 2000 rpm. At 1000 rpm, the size of the largest particles is found 168 micron and the smallest one is 29.8 micron.

Figure 3.6 shows the microparticles at x500 magnification and visibly it is clear that the microparticles produced at the higher rpm are smaller than the microparticles produced at the lower rpm. At 1700 rpm, the size of the large particle is 70 micron (Fig 3.6 B) and at 2000 rpm, it is 57 micron (Fig 3.6 C).

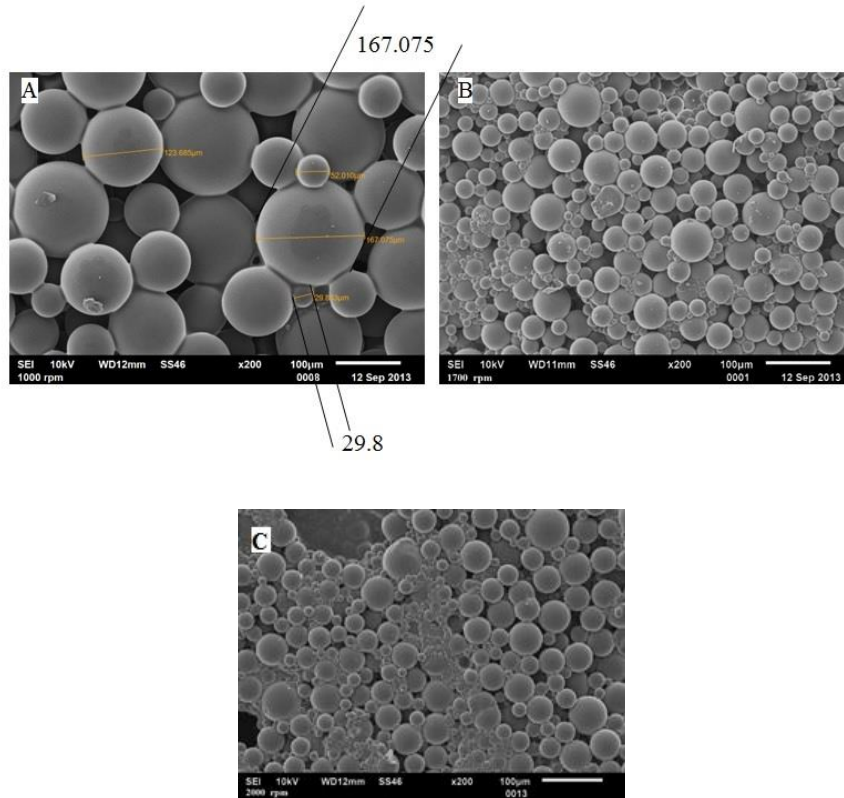


Figure 3.5- Scanning electron microscopy images showing visual size difference agitated at three different RPM: (A) 1000 RPM, (B) 1700 RPM, and (C) 2000 RPM at x200 magnification.

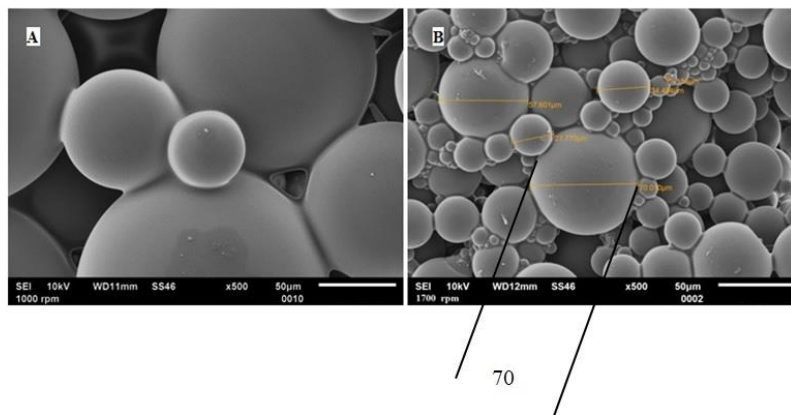
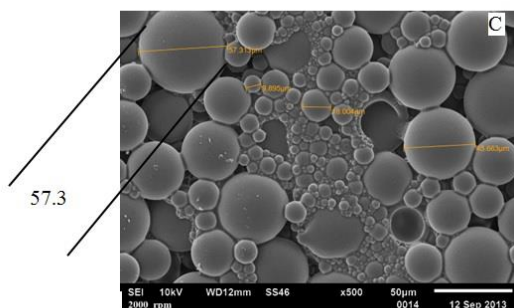


Figure 3.6 Scanning electron microscopy images showing visual size difference agitated at three different RPM: (A) 1000 RPM, (B) 1700 RPM, and (C) 2000 RPM, at x500 magnification.



(Figure 3.6 continued)



As the rotational speed increases mean diameter decreases, and more small particles are observed in the microscopic images. The size of the smallest particles was not possible to determine at x200 and x500 magnification for 1700 and 2000 rpm. Figure 3.7 shows the images at higher magnification (x2000 and x6000). At 1700 rpm the smallest particle is less than 1 micron (Figure 3.7 A, x2000 magnification) and at 2000 rpm more small particles are detected (Figure 3.7 B, x2000 magnification). To determine the smallest particle size x6000 is used (for 2000 rpm) and it is found that many particles are even smaller than 1 micron (Figure 3.7C). Overall Figure 3.7 describes the observable morphology and sizes of the microparticles produced at different rotational speed of the propeller and observed at higher magnification. On the basis of these three Figures (Figure 3.5, 3.6 and 3.7) and the smooth spherical shape of the microparticles, it can be said that the surface morphology of the resultant microparticles is not affected by the rotational speed over the range tested.

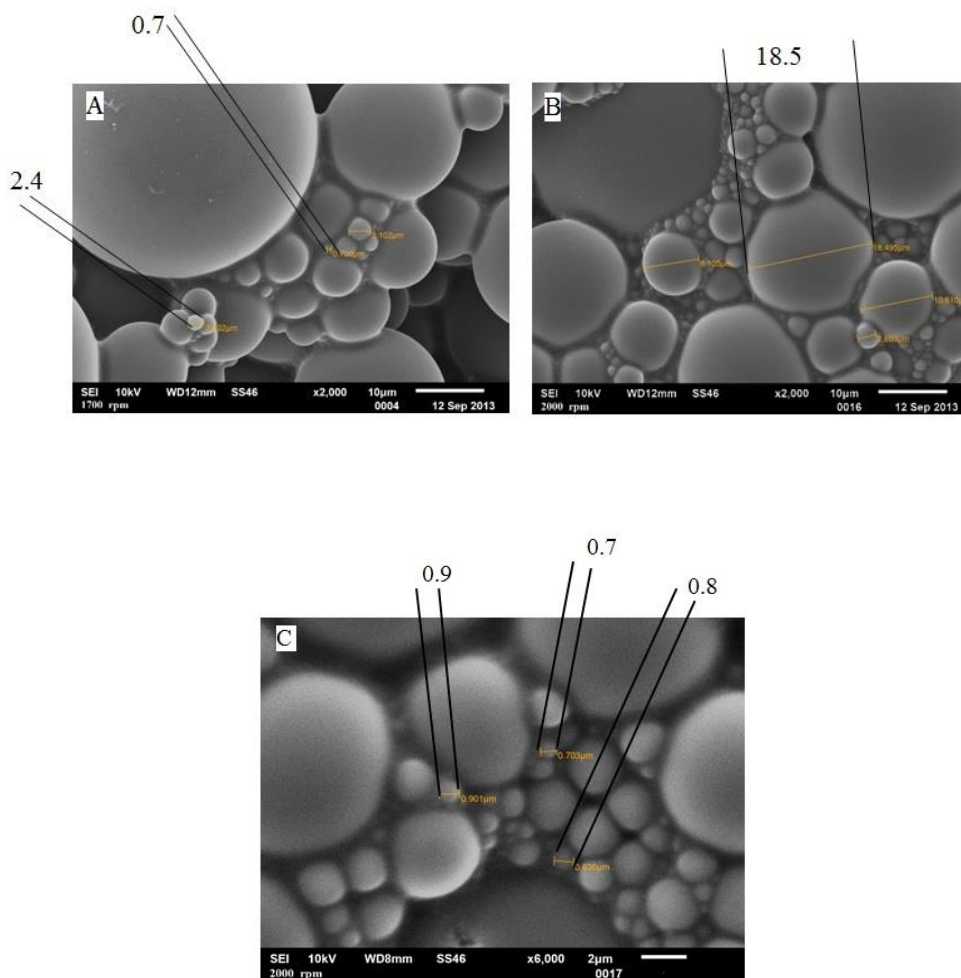


Figure 3.7 Scanning electron microscopy images showing small microparticles prepared at (A) 1700 RPM (x2000 magnification) (B),(C) 2000 RPM (x2000 and x6000 magnification).

### 3.3.2 Size Distribution

Optical microscopy visible properties of the microparticles have been quantified as the mean diameter and the size distribution. Using different agitation rates including 300, 500, 800, 1000, 1200, 1500, 1700, and 2000 RPM, size distributions have been determined and showed in Figure 3.8.

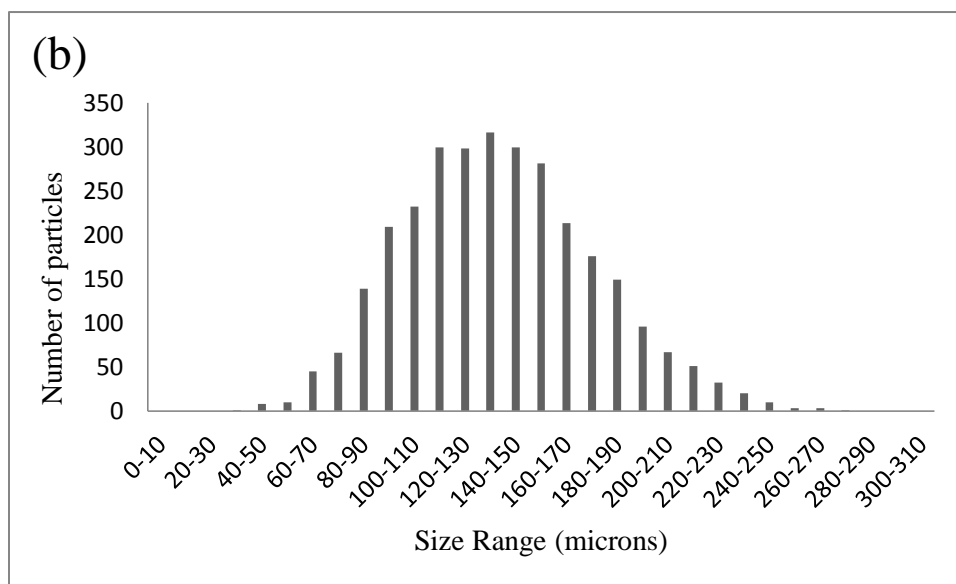
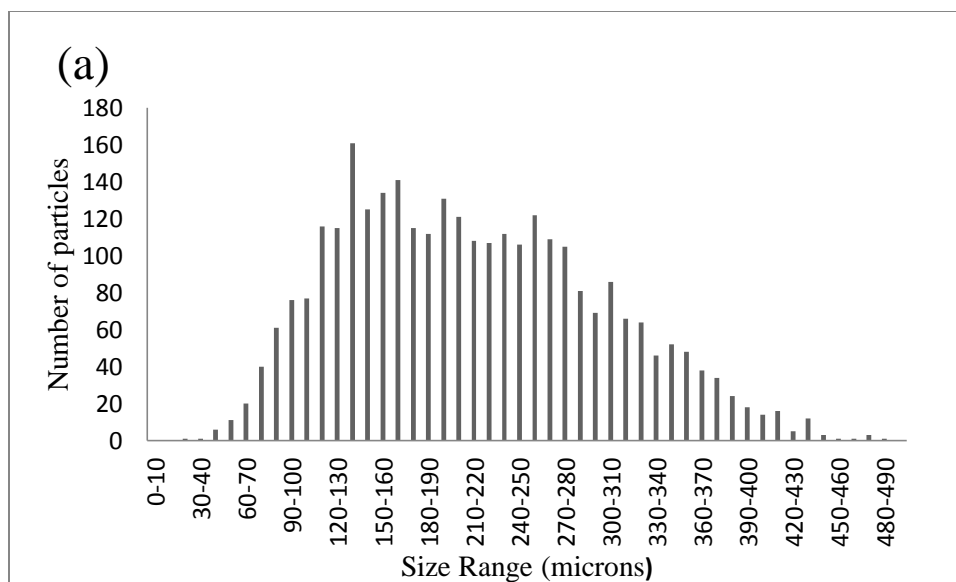
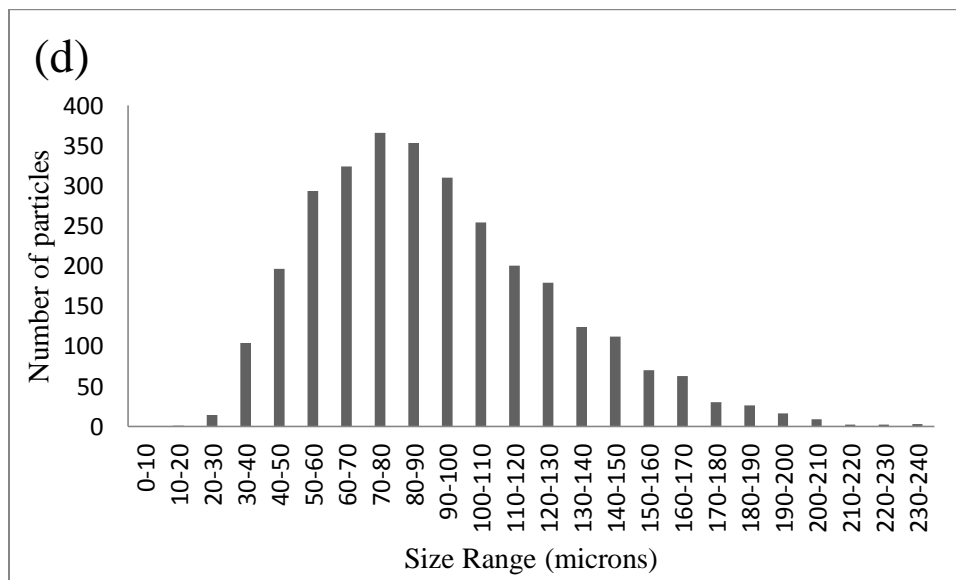
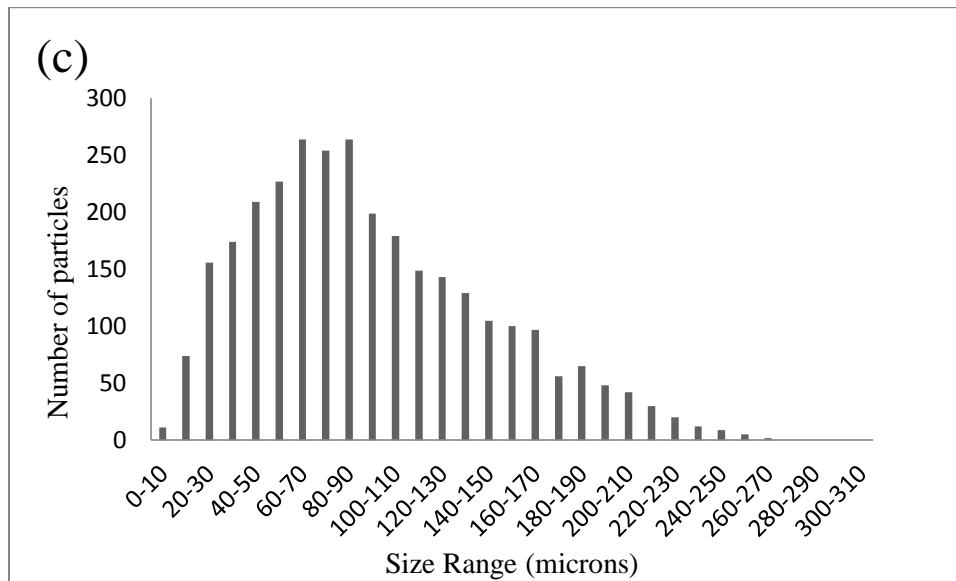
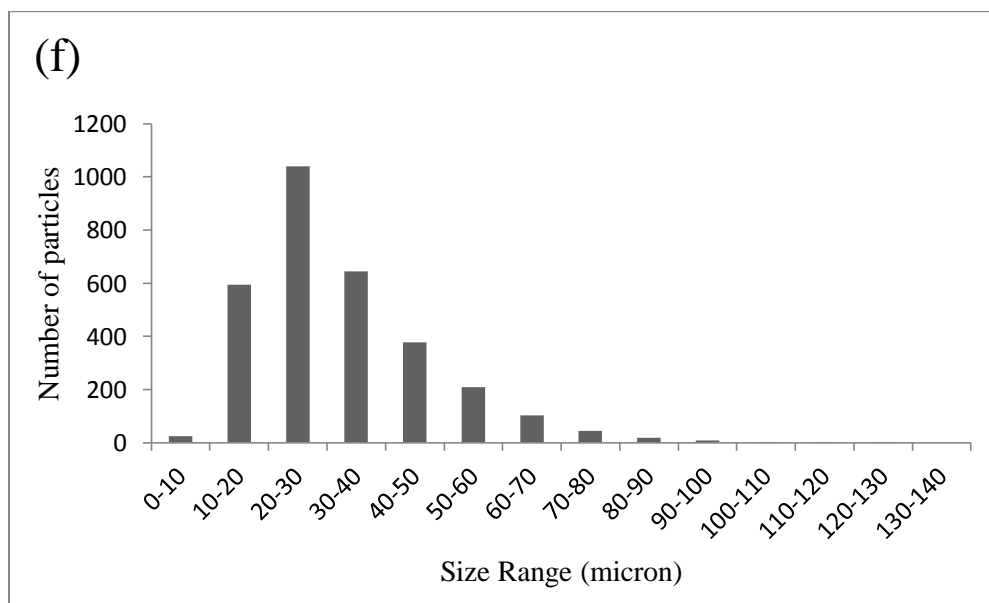
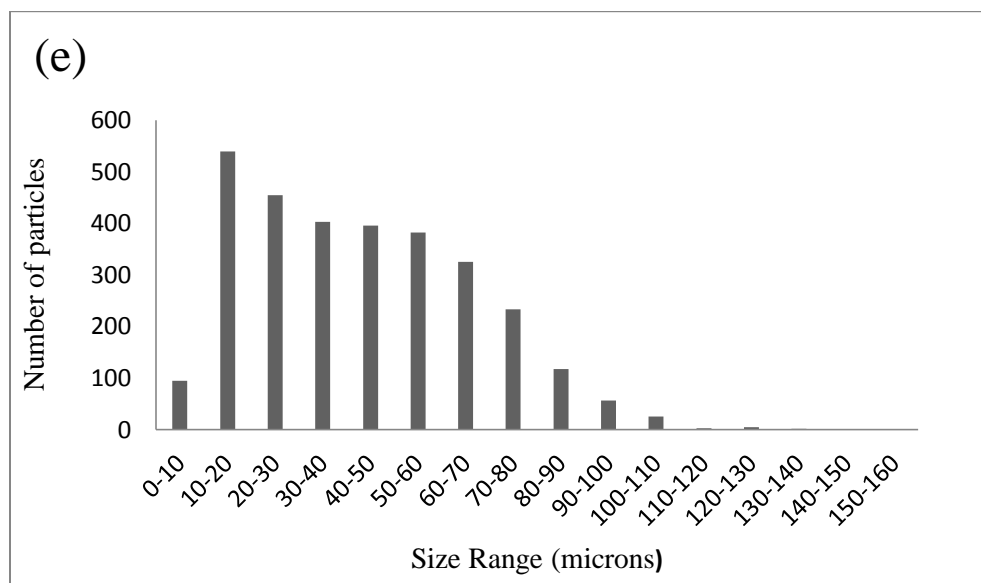


Figure 3.8 Size distribution of the microparticles prepared at (a) 300, (b) 500, (c) 800, (d) 1000, (e) 1200, (f) 1500 and (g) 1700 RPM using the reactor with the impeller

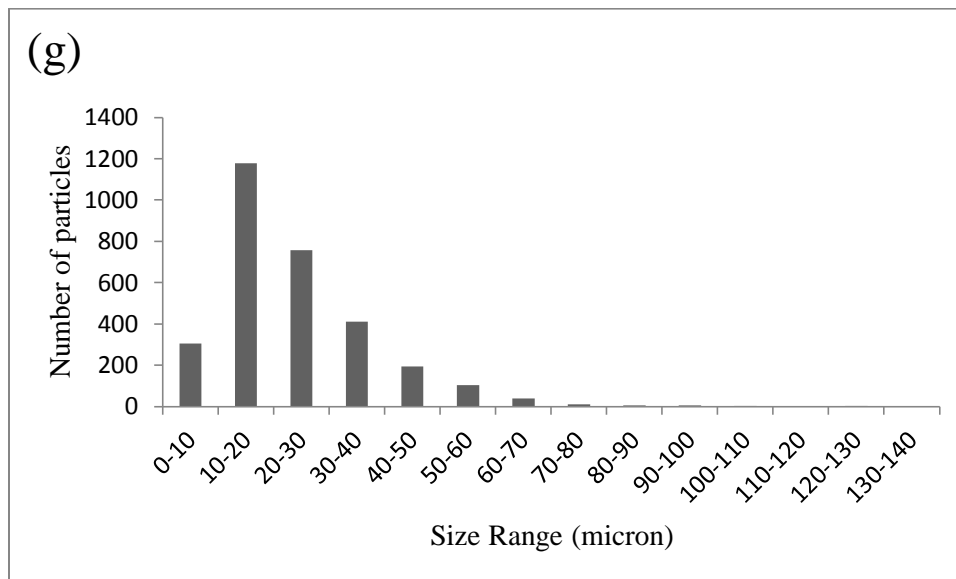
(Figure 3.8 continued)



(Figure 3.8 continued)



(Figure 3.8 continued)



Size distributions of the particles produced using the oscillatory reactor at three different oscillation amplitudes (5 mm, 7.5 mm and 10 mm) and corresponding frequencies have been illustrated in Figure 3.9, 3.10 and 3.11.

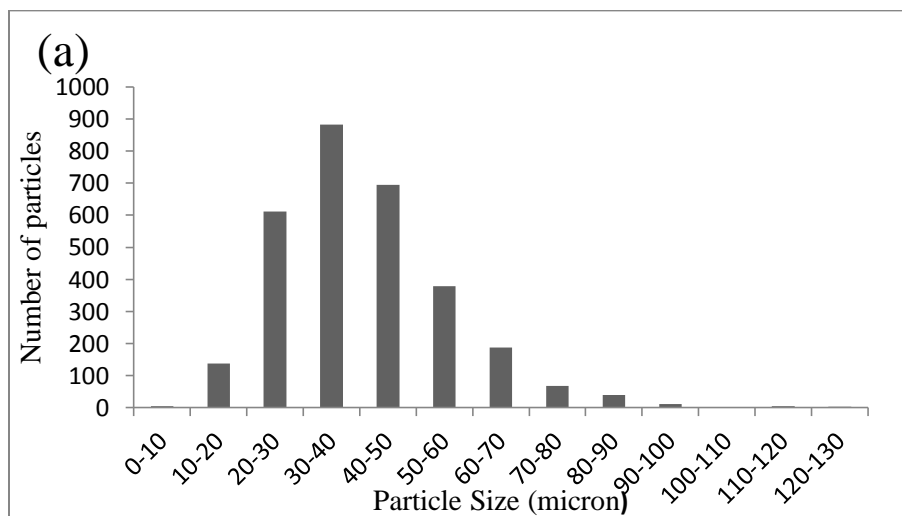
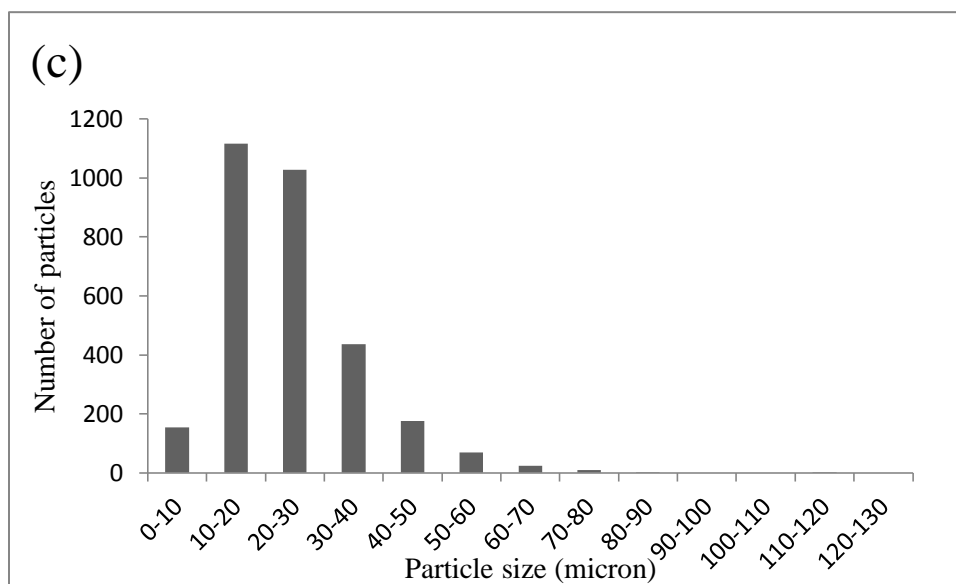
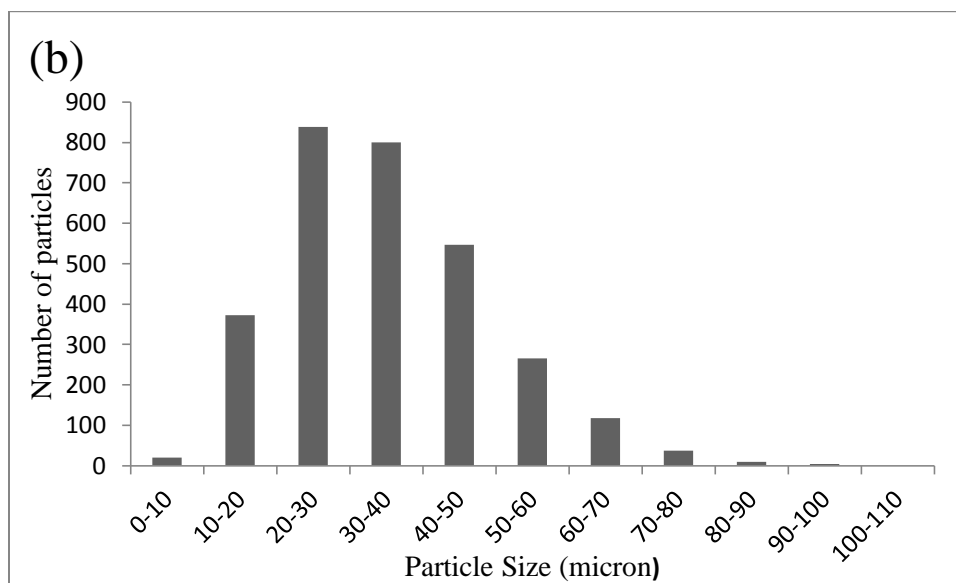


Figure 3.9 Size distribution of the microparticles prepared at (a) 4.3, (b) 7.1, (c) 10.6, (d) 14, (e) 17.6 Hz frequencies and 5 mm oscillation amplitude

(Figure 3.9 continued)



(Figure 3.9 continued)

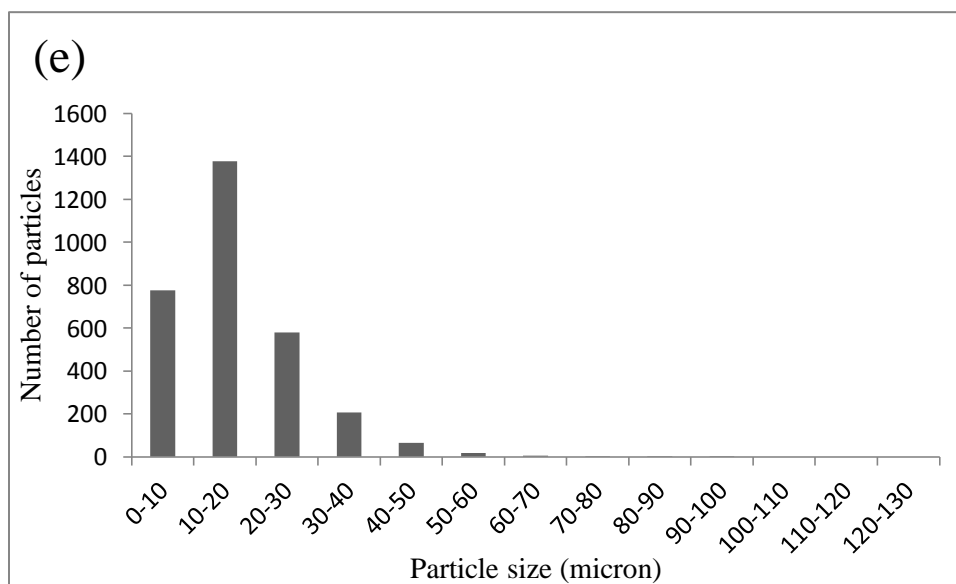
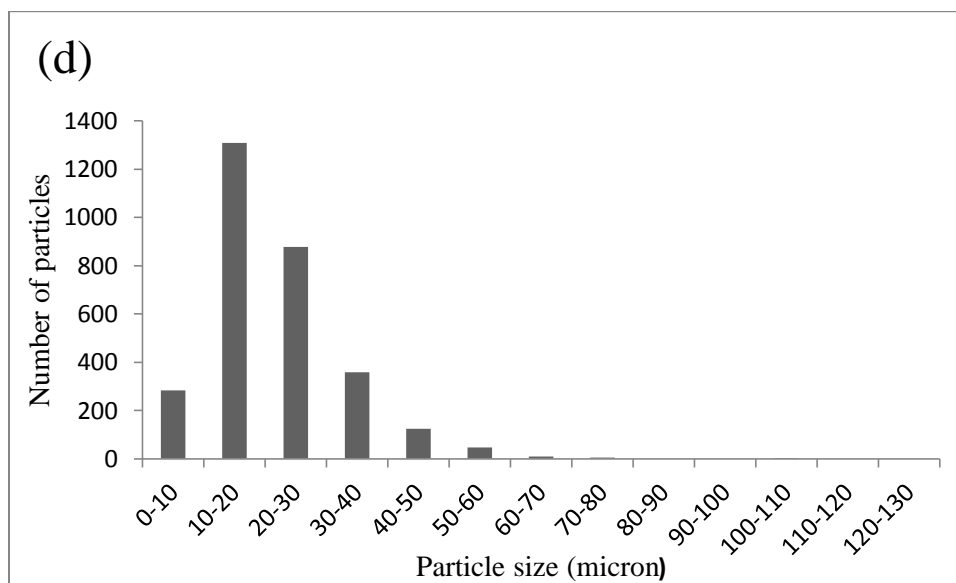




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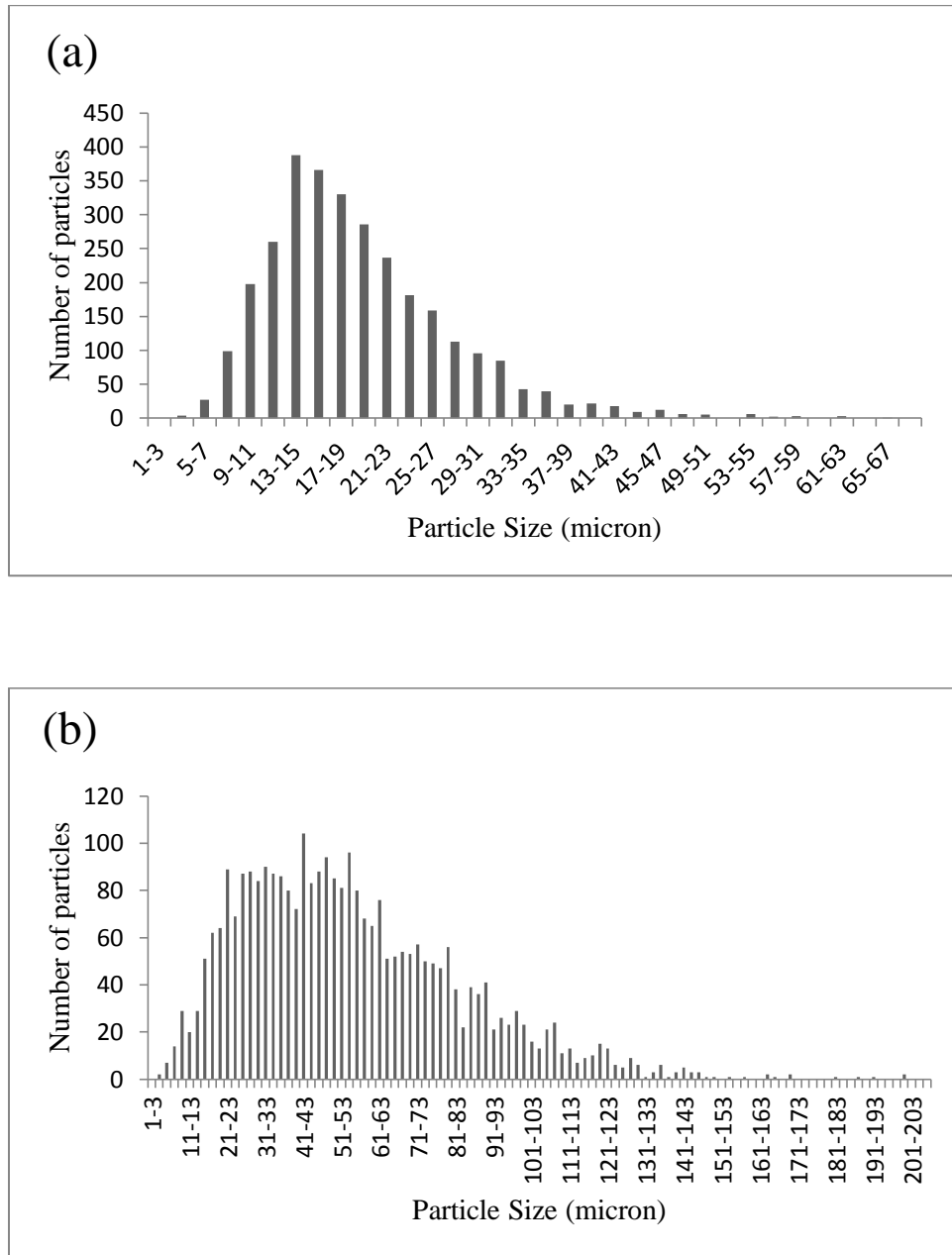
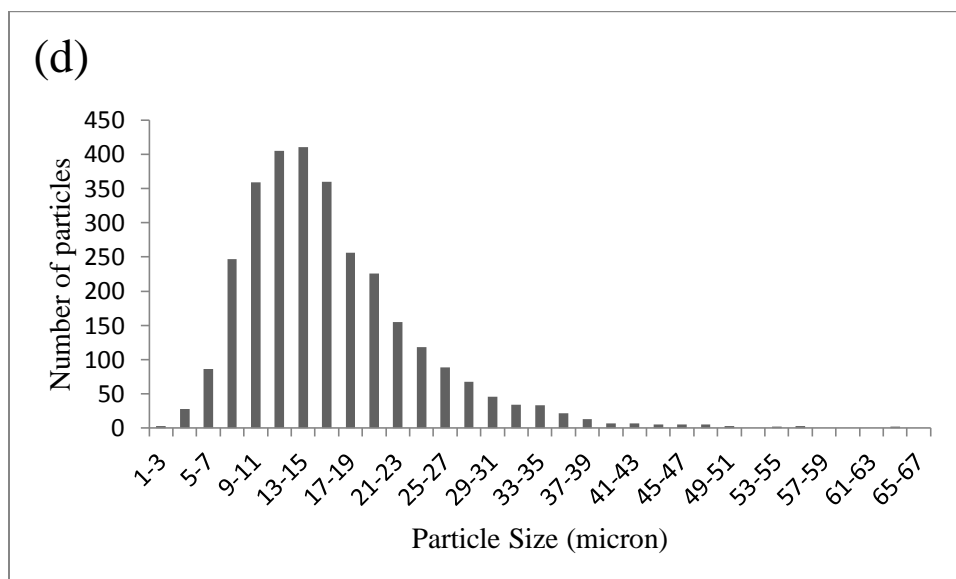
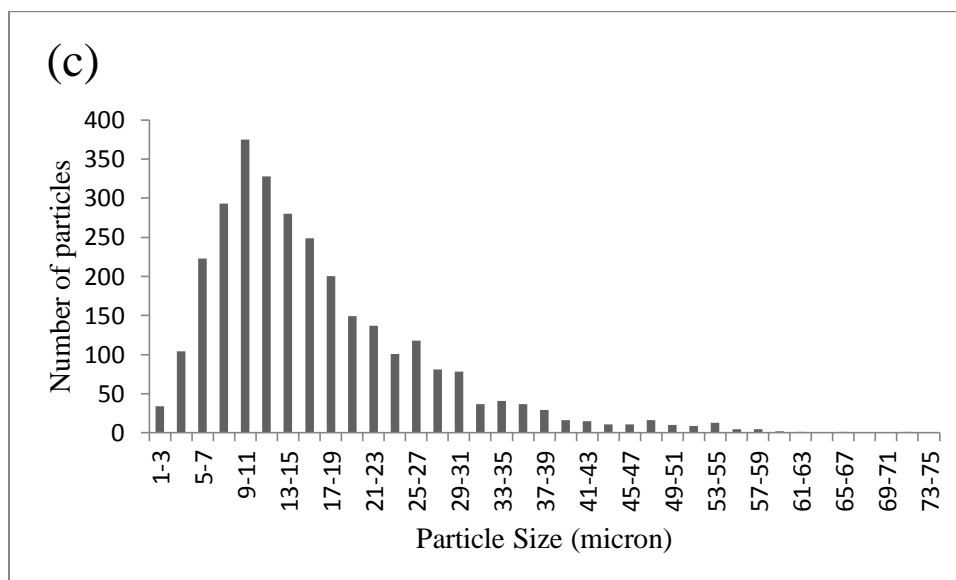


Figure 3.10 Size distribution of the microparticles prepared at (a) 3.3, (b) 5.4, (c) 7, (d) 8, (e) 10.7, (f) 13.4 Hz frequencies and 7.5 mm oscillation amplitude

(Figure 3.10 continued)



(Figure 3.10 continued)

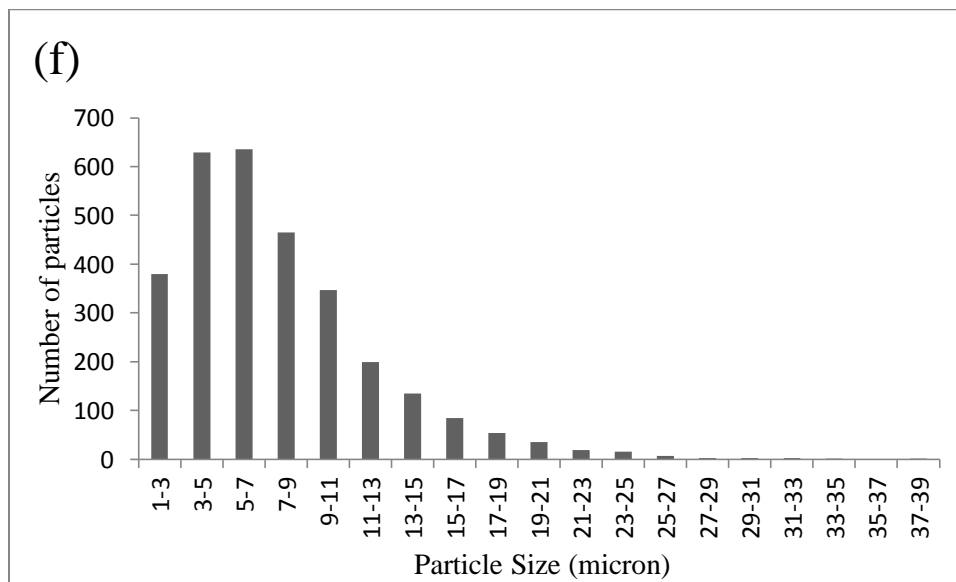
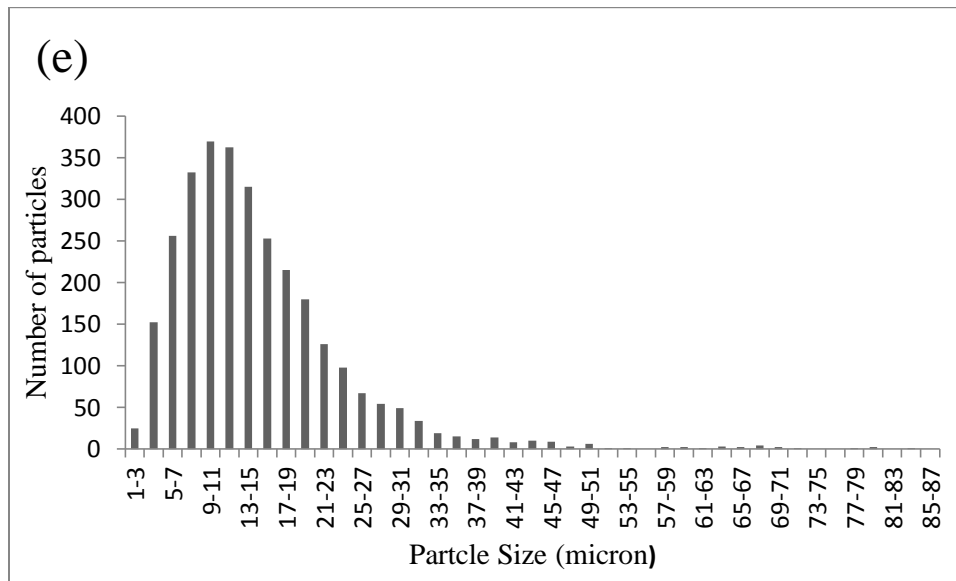


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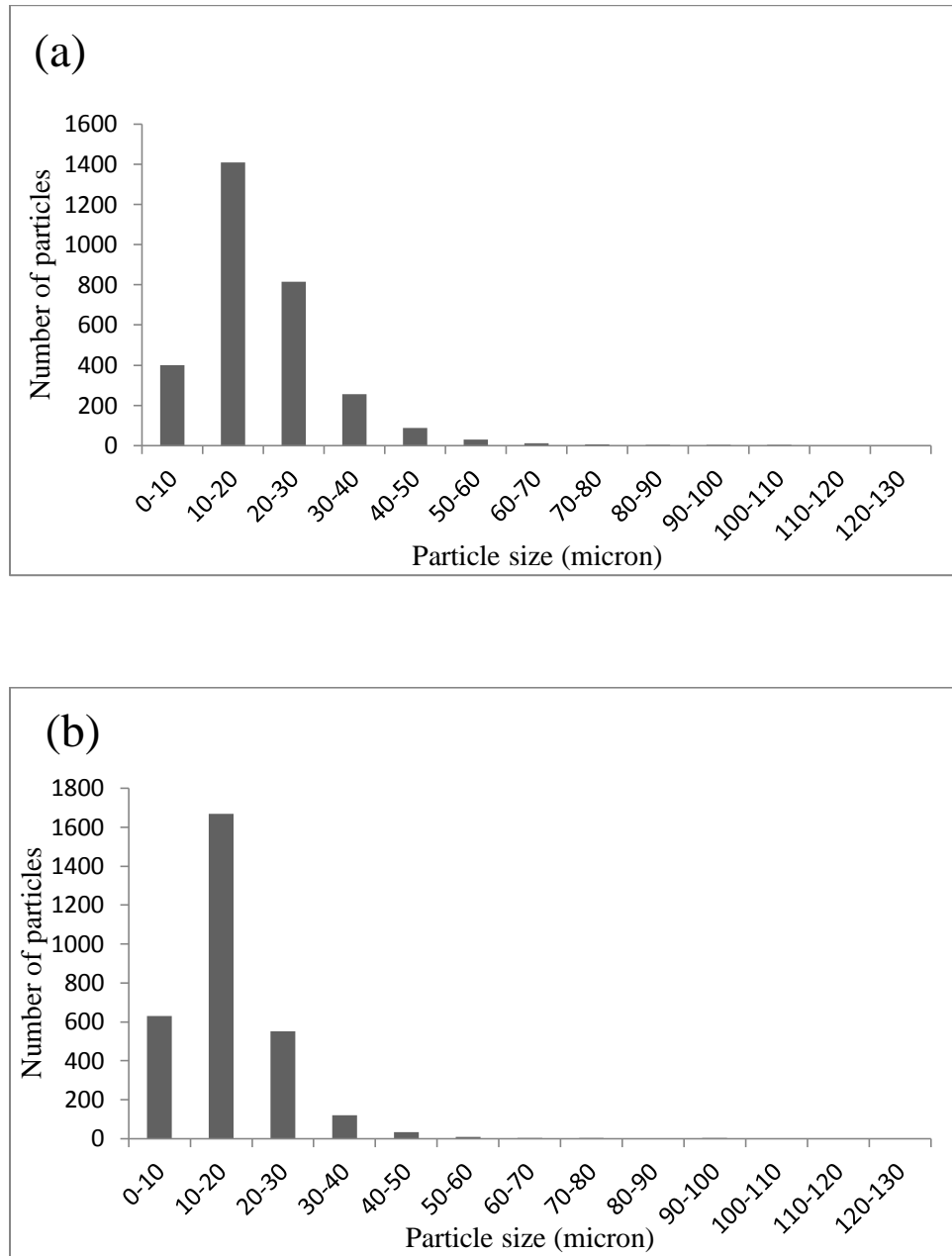
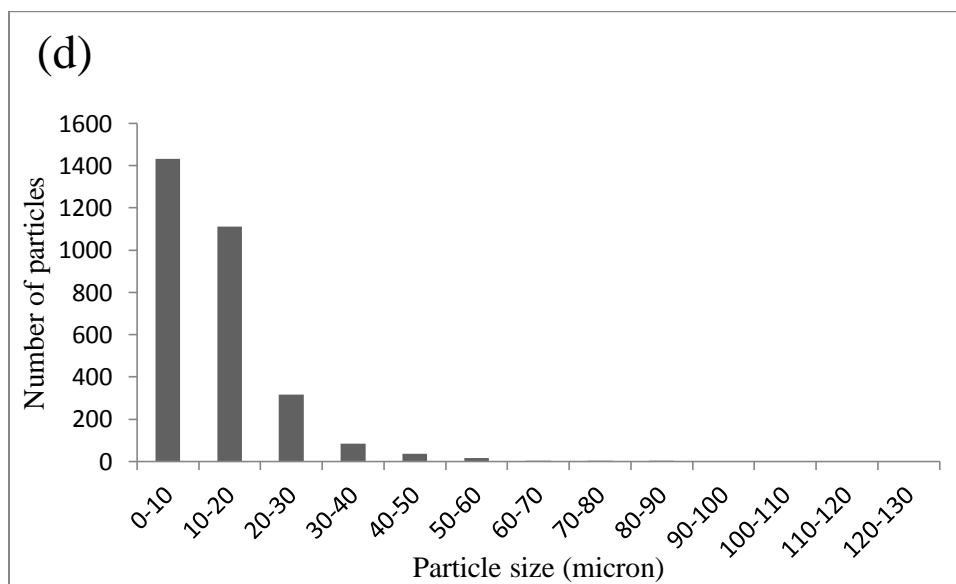
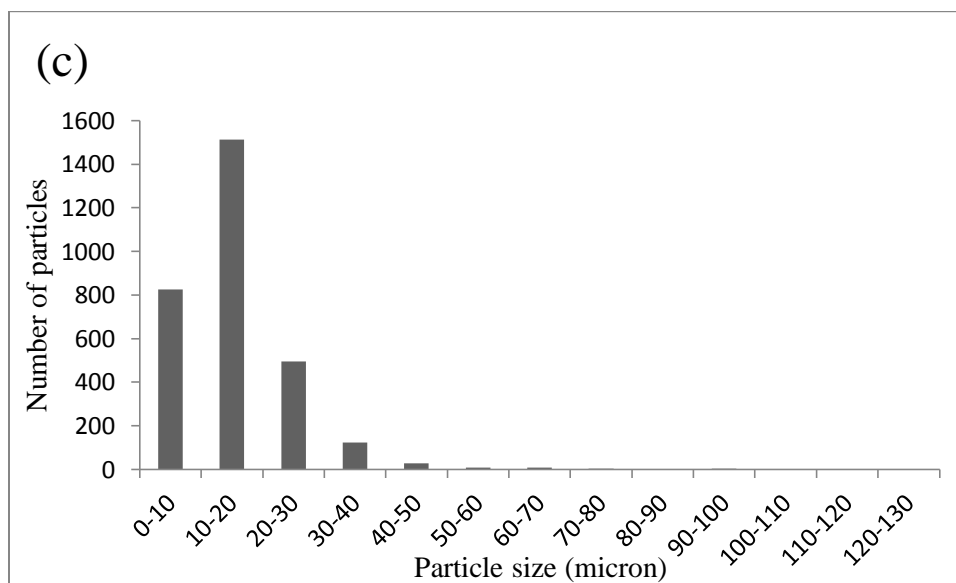
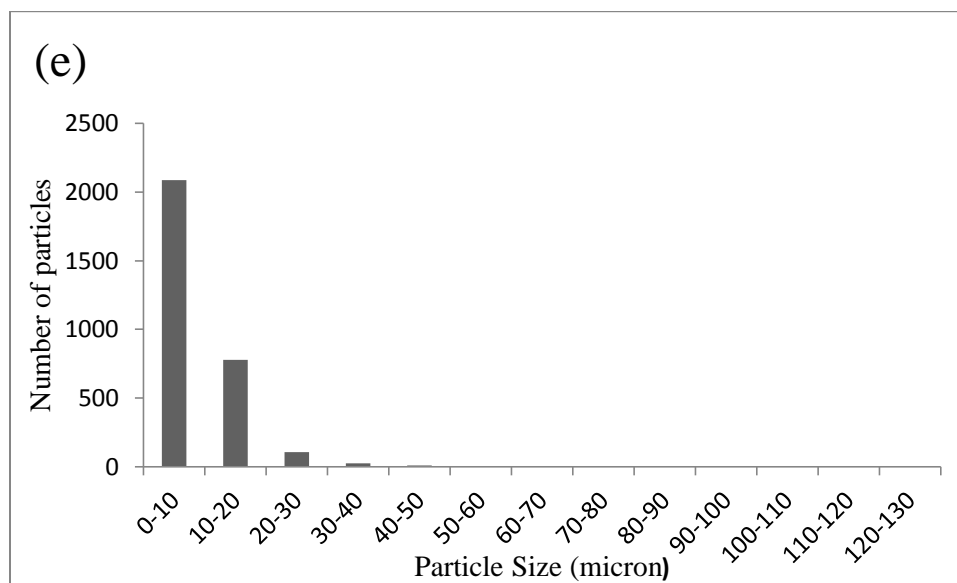


Figure 3.11 Size distribution of the microparticles prepared at (a) 2.7, (b) 4.5, (c) 6.7, (d) 8.8, (e) 11.6 Hz frequencies and 10 mm oscillation amplitude

(Figure 3.11 continued)



(Figure 3.11 continued)



Agitation rate from 300 rpm to 2000 rpm has a significant effect on size distribution. The microparticles prepared with high agitation speed are considerably small than those prepared with low agitation speed. High stirring rate aids large droplets to be broken into smaller droplets. Figure 3.12 illustrates the proportional relationship between the stirring rate and particle size. As the agitation speed increases, the size of the particles decreases, and at 1700 rpm, the narrowest size distribution has been obtained. This inverse relationship between the stirring rate and particle size distribution has been reported in some other scientific studies (Valot et al., 2009; Wei et al., 2011). The plot can be separated into three sections; the first one is below 500 rpm where the size distribution area is broad. At a lower agitation rate, the tendency of the droplets to coalesce and aggregate is high and the outcome is larger mean particle size and a wide size distribution. The second region lies within 500 rpm to 1000 rpm stirring speed, where the

distribution is more compact than the first section. Finally above 1000 rpm, the size distribution is narrower than the other two regions, which results from the higher power input.

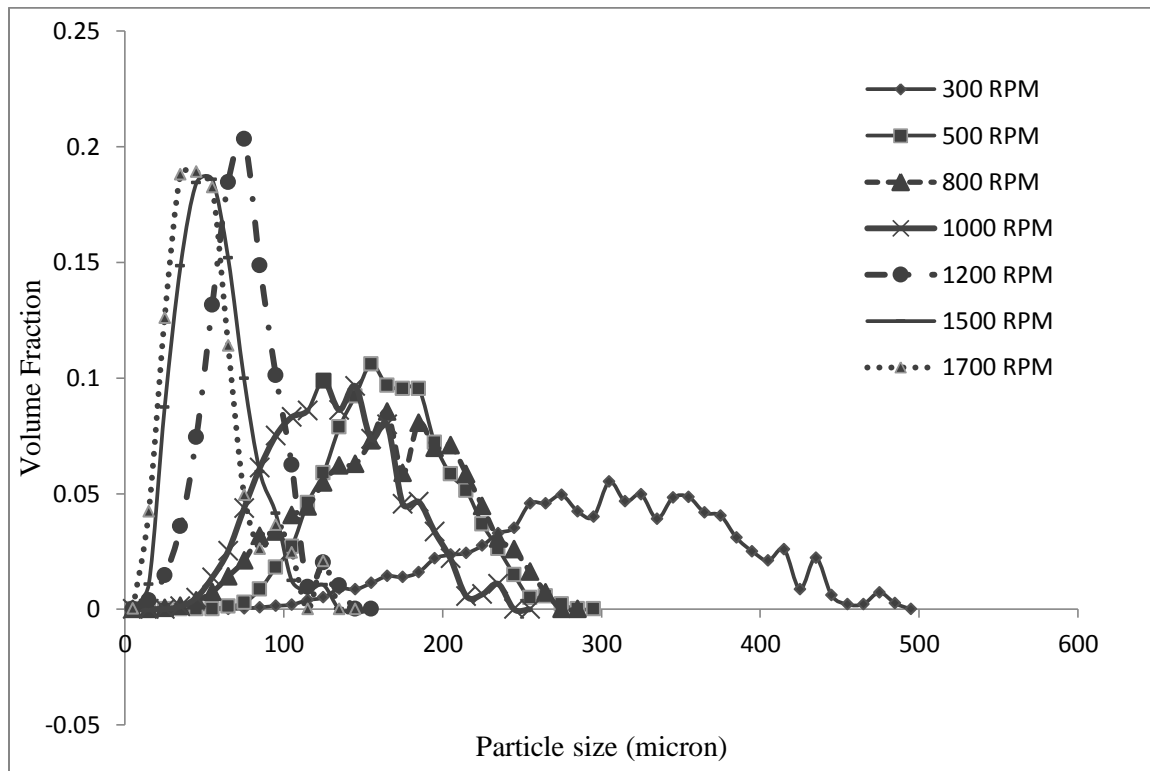


Figure 3.12 Particle size distributions as a function of stirring rate used during microencapsulation

The mean diameter also decreases with the increasing stirring rate. In the Figure 3.13 shows the effect of stirring rate on mean particle size. Between 300 rpm (0.055 W/Kg) and 1000 (2.03 W/Kg) rpm, the mean diameter decreases significantly from 215 micron to 92 micron. But between 1200 rpm (3.5 W/Kg) and 1700 rpm (10 W/Kg), the mean diameter decreases from 43 micron to 19 micron. Above 1200 rpm the mean diameter changes to a lesser extent.

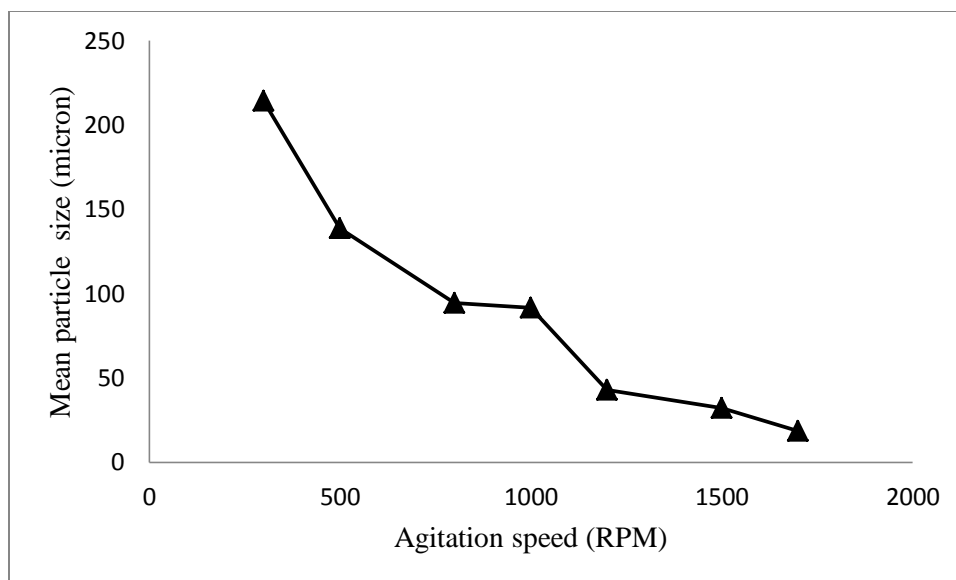


Figure 3.13 Mean microparticle size as a function of stirring rate used during microencapsulation

### 3.3.3 Effect of Oscillation Amplitude and Frequency

In a piston driven oscillatory reactor, the mixing intensity is controlled by the oscillation amplitude and frequency. To evaluate the individual effect of oscillatory amplitude and frequency, experiments were conducted by varying one of the parameters and keeping the other constant. Three different amplitudes (5mm, 7.5mm and 10mm) with a range of frequencies have been used. Figure 3.14 depicts the results: Figure 3.14(a) 5 mm amplitude, Figure 3.14(b) 7.5 mm amplitude and Figure 3.14(c) 10 mm amplitude. At constant amplitude several experiments have been conducted using different oscillation frequency. As the oscillation frequency increases, the peak of the size distribution increases in height giving a narrower distribution whereas the tail of the distribution appears to be short. These phenomena explain that the distribution is narrower and even more uniform sized particles are likely to be found. With the increase of oscillation frequency the energy dissipation of the system i.e. the turbulence in the system also increases, which results into the formation of more uniform and small droplets.



Mean particle size also decreases (from 41 micron to 17 micron) as the oscillation frequency increases from 4.3 to 17.6 Hz at 5 mm amplitude. At 7.5 mm and 10 mm amplitude, mean particle size decreases with the increasing frequency (Figure 3.15).

Several studies have shown that oscillation frequency and amplitude play a major role in controlling the particle size and size distribution (Ni et al., 1998; Pereira et al., 2001). In Figure 3.16, the effect of oscillation amplitude on the mean particle size for a fixed oscillation frequency of  $11 \pm 0.6$  Hz has been presented. The oscillation amplitude and oscillation frequency show similar effect on mean particle size.

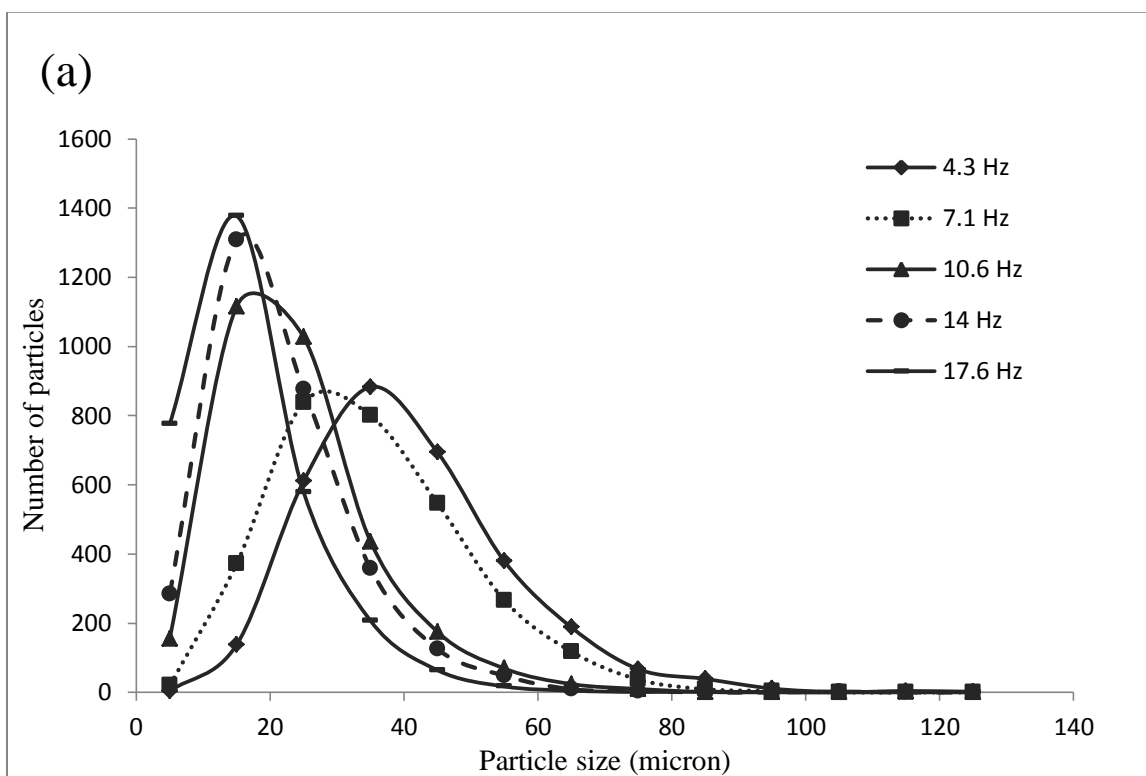
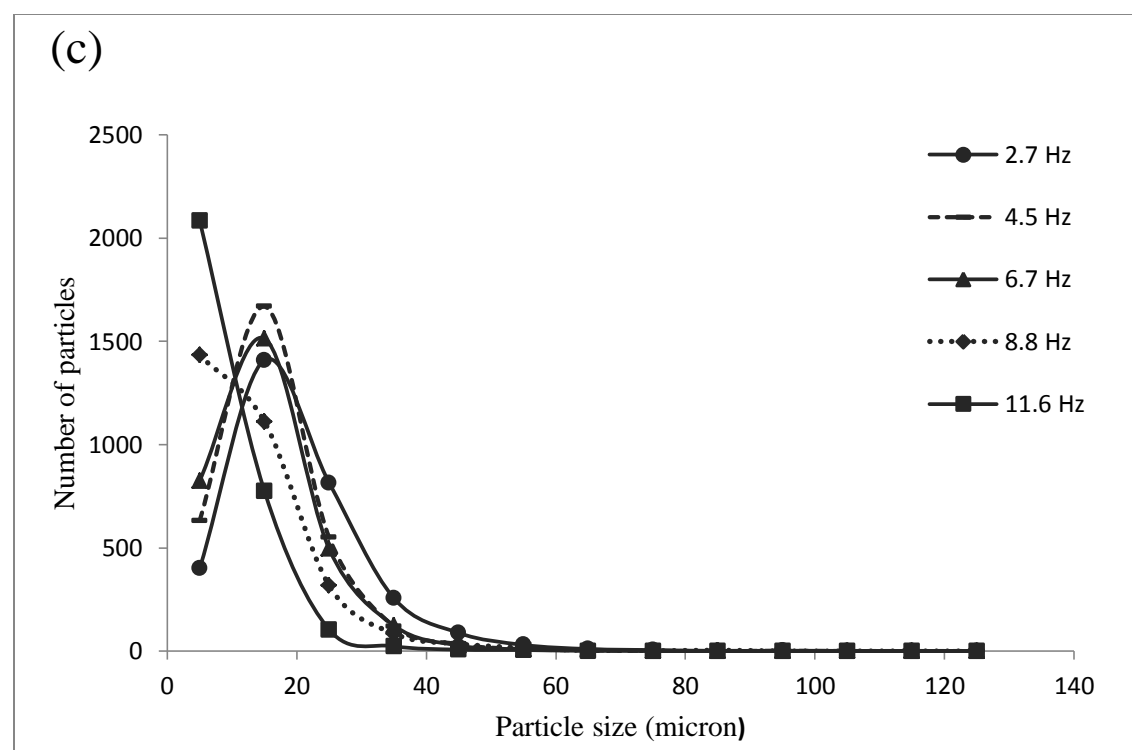
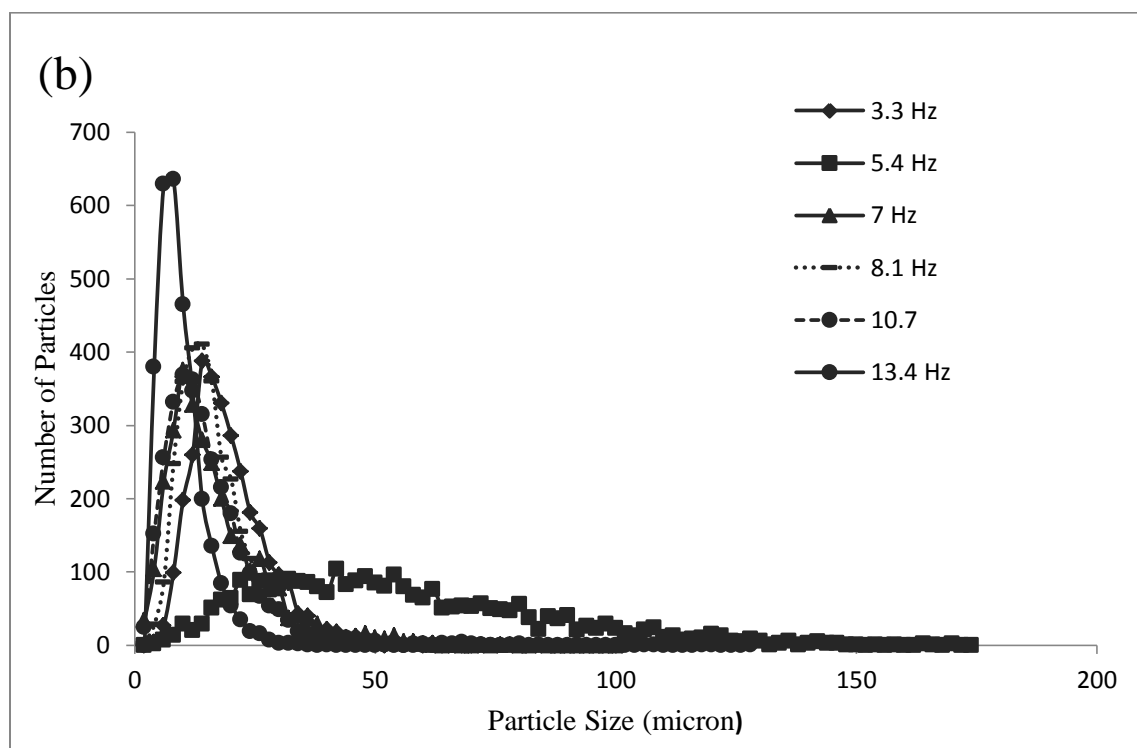


Figure 3.14 Particle size distribution as a function of oscillation frequency used during microencapsulation at a constant oscillation amplitude (a) 5 mm (b) 7.5 mm and (c) 10 mm

(Figure 3.14 continued)



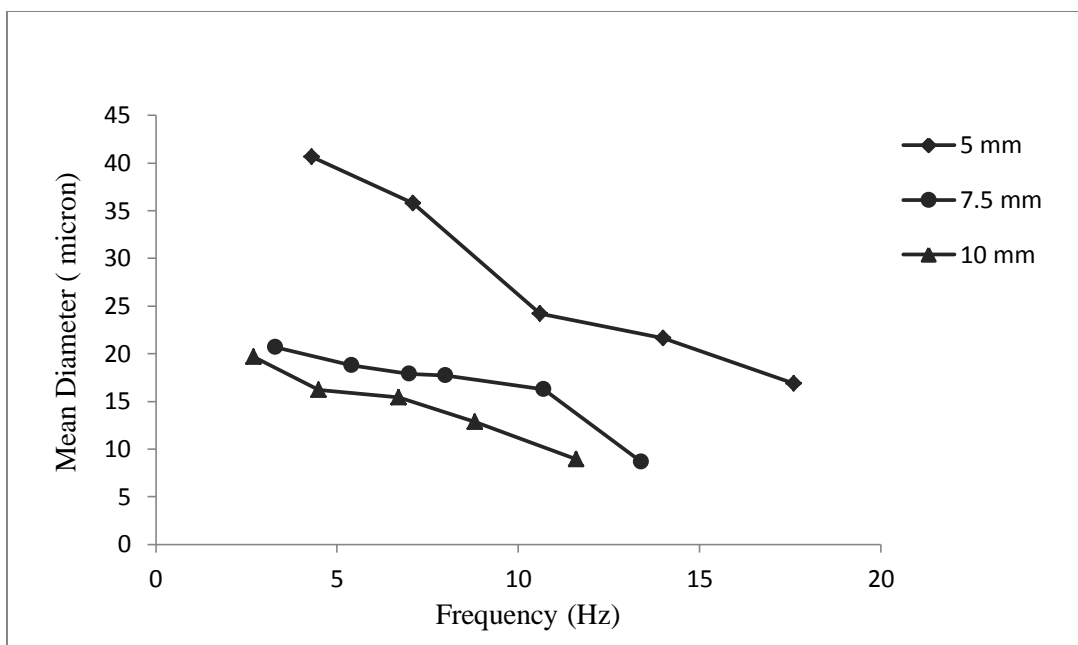


Figure 3.15 Mean particle size as a function of oscillation frequency used during microencapsulation at constant oscillation amplitude (5 mm, 7.5 mm and 10 mm)

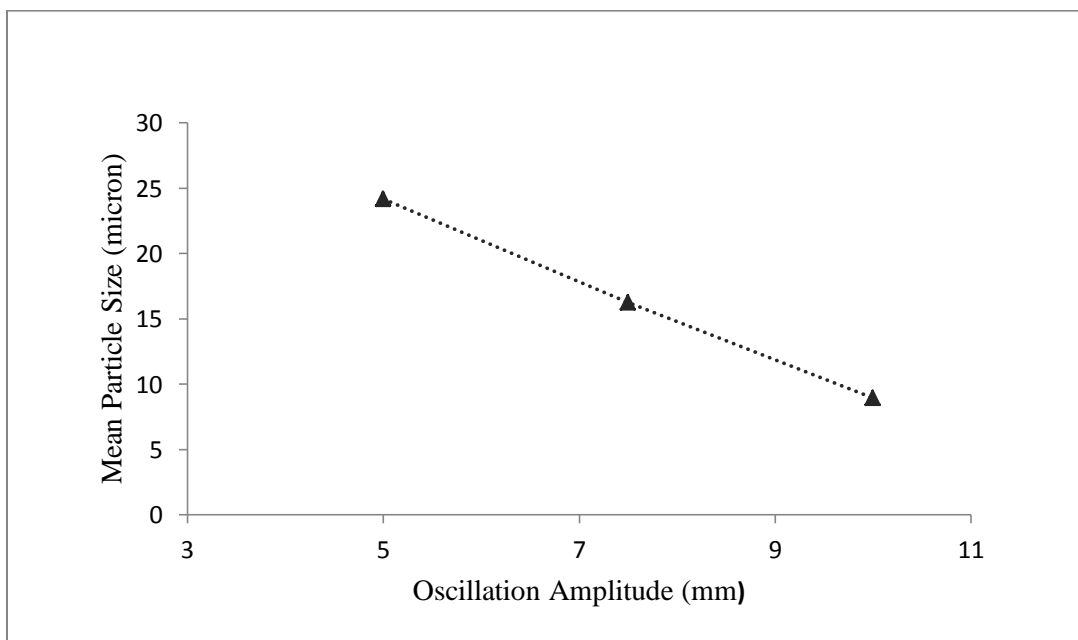


Figure 3.16 Mean particle size as a function of oscillation amplitude at a constant oscillation frequency ( $11 \pm 0.6$  Hz)

### **3.3.4 Effect of Surfactant Concentration**

A surfactant or stabilizer can prevent the coalescence of droplets during emulsification. The stabilizer plays an important role in the synthesis of individual spherical microparticles. Surfactants or stabilizers generally stabilize the system by stabilizing the droplets formed through a combination of interfacial tension reduction and increasing the repulsion between the droplets when they collide through preventing them from coalescence (Yuan et al., 2009). The choice and concentrations of the surfactants depend on the desired microparticle size and characteristics, the type of solvent used and the nature of the surfactants. Low toxicity, good solubility and suitability in a wide range of molecular weight have made PVA (Polyvinyl alcohol) the most common surfactant used in the formation of microparticles of relatively small size and uniform size distribution (Sahoo et al., 2002). The purpose of this study is to assess the effect of PVA concentration on the size distribution of microparticle. A number of previous studies have shown that, PVA concentration in the aqueous phase has a significant effect on the size and size distribution of the microparticles (Sahoo et al., 2002; Yuan et al., 2009). Generally 1.28% PVA has been emulsified in the aqueous phase. For the purpose of study, microparticles have been produced using various amount of PVA ranging from 0.2% to 2% in the aqueous phase and the mean particle size as a function of PVA concentration has been presented in Figure 3.17. It clearly shows that the mean microparticle size has been decreased from 98 micron to 56 micron with an increase in the PVA concentration. Different concentrations of PVA may be responsible for the differences in the stability of the system. High concentration of PVA reduces the interfacial tension of the droplets by orienting the PVA molecules at the organic solvent/water interface. A significant increase in the net shear stress at a constant energy density

results, and smaller droplets are likely to be found, which resulted the decrease in the mean particle size (Song et al., 2008).

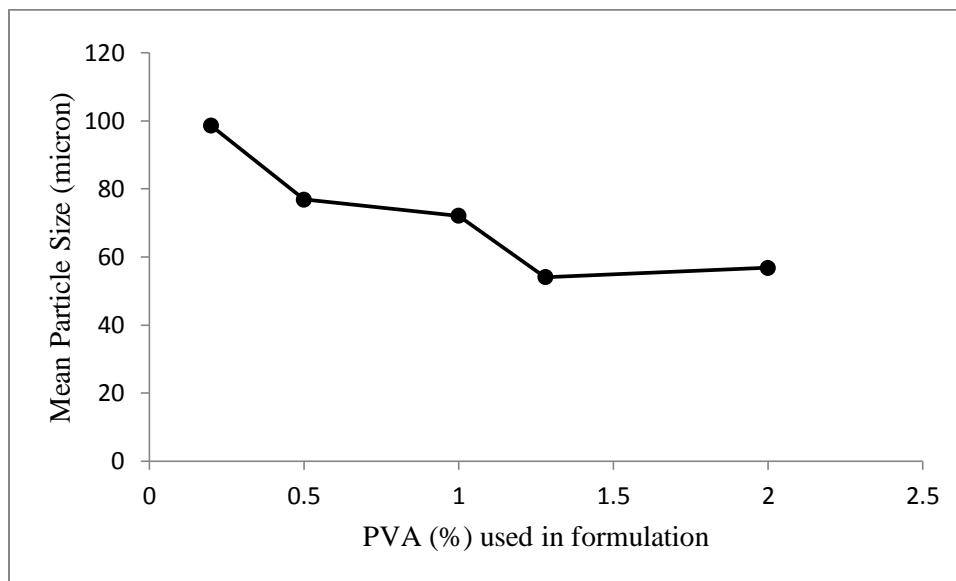


Figure 3.17 Mean particle size as a function of PVA concentration

### 3.3.5 Energy Dissipation Calculation and Comparison of the Reactors

In this section the mean particle size and size distribution has been represented in terms of turbulence dissipation energy. Using Equation 2 and 3 from the Section 3.2.4.3, power input per unit mass for each type of reactor has been calculated. The propeller Reynolds number (14000-82000) indicates that the flow is turbulent. The power number is taken as 0.5 to calculate the energy dissipation per unit mass for the reactor with a three-blade propeller. The volume is converted to a mass assuming the density of water, as the most part of the volume is water in order to avoid complication. This mass is used in the calculations. Table 3.1 presents the associated energy dissipation rate per unit mass for the reactor with a propeller for different rotational speeds. From the values of particle size, it is seen that with the increase of the stirring

rate the distribution becomes more compact. In Table 3.2, energy dissipation rate and associated size parameters are presented. Energy dissipation per unit mass is slightly lower for the reactor with propeller than the oscillatory reactor, but the size distribution is wider. In Figure 3.15, particle size distribution for two types of reactor at 1000 rpm or 16.7 Hz (at 5 mm amplitude) has been shown. For the reactor with a propeller, the average particle size is  $91.73 \pm 35.88$  micron, whereas for the oscillatory reactor it is  $16.87 \pm 9.75$  micron. Comparison between the two tables and Figure 3.18 satisfactorily explains that, a compact size distribution and small mean particle size are the two vital aspects of the oscillatory reactor, which makes it more suitable than the reactor with propeller. The reactor with propeller and the oscillatory reactor differ from one another in terms of energy dissipation into the reactor fluid. Even for the same power input 0.25 W/Kg, the mean particle size is 139 micron for the reactor with three-blade propeller (at 500 rpm), whereas the mean particle size for the piston driven reactor is 41 micron (at 5 mm amplitude and 4.3 Hz frequency). The propeller transfers the energy along the direction of the blades, which results into uneven energy transfer at different points along the blade. This may lead to a broad size distribution of the microparticles. Increasing the stirring speed can help to control the size distribution up to a certain critical power level. Beyond this power level the capsules formed are broken down and terminate the reaction from taking place. But in case of the oscillatory reactor, the energy transfers uniformly across the piston cross section into the reactor fluid. In terms of particle size and size distribution, oscillatory reactor is more suitable than the reactor with propeller to attain a desired particle size distribution.

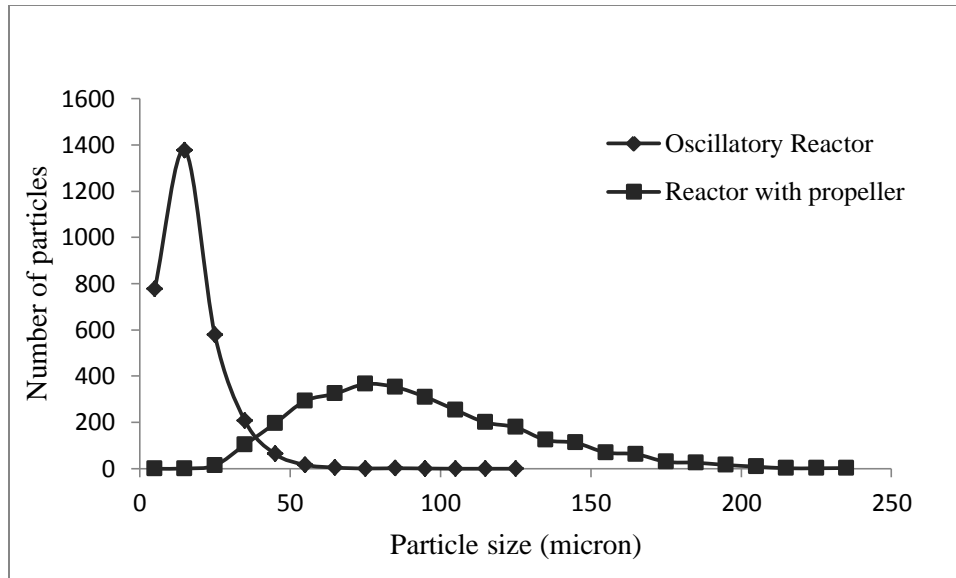


Figure 3.18 Particle size distributions for two types of reactor at 1000 rpm

Table 3.1 and 3.2 are given below:

Table 3.1: Energy dissipation rate and particle size for the reactor with three blade propeller

Stirring rate (RPM)	Power (W/Kg)	Mean particle size (micron)	Maximum particle size (micron)	Minimum particle size (micron)
300	0.055	215	478	22
500	0.25	139	456	32
800	1.04	95	269	9
1000	2.03	92	234	20
1200	3.51	43	133	6
1500	6.86	33	129	8
1700	10	19	117	2

Table 3.2: Energy dissipation rate and particle size for the oscillatory reactor

Oscillation frequency (Hz)	Oscillation Amplitude (mm)	Power (W/Kg)	Mean particle size (micron)	Maximum particle size (micron)	Minimum particle size (micron)
4.3	5	0.25	41	130	6
7.1		1.11	36	154	5
10.6		3.7	25	177	4
14		8.5	22	106	2.8
17.6		16.2	17	99	2
3.3	7	0.25	21	168	5.6
5.4		1.11	19	199	3.8
7		2.4	18	152	3
8		3.7	18	103	2
10.7		8.5	17	127	1.2
13.4	10	16.7	8	80	1.3
2.7		0.25	20	106	3.4
4.5		1.11	16	96	1.8
6.7		3.7	15	97	2.5
8.8		8.5	12	87	1.4
11.6		16.2	8	77	1.3

For the same energy dissipation rate, experiments have been conducted for different frequencies and different amplitudes. The resultant mean particle size is shown in the Figure 3.19. For the same amount of power consumption per unit mass such as 3.7 W/Kg, mean particle size are different for different amplitude. For high amplitude (10 mm) mean particle size is 15 micron, for 7.5 mm and 5 mm amplitude mean particle size are 18 and 25 micron respectively. With the increase of the oscillation amplitude, mean particle size decreases even when the power input is same. The reason behind this may be the shear impact of the oscillation increases with the increase in oscillation amplitude resulting more small droplets during the mixing process.



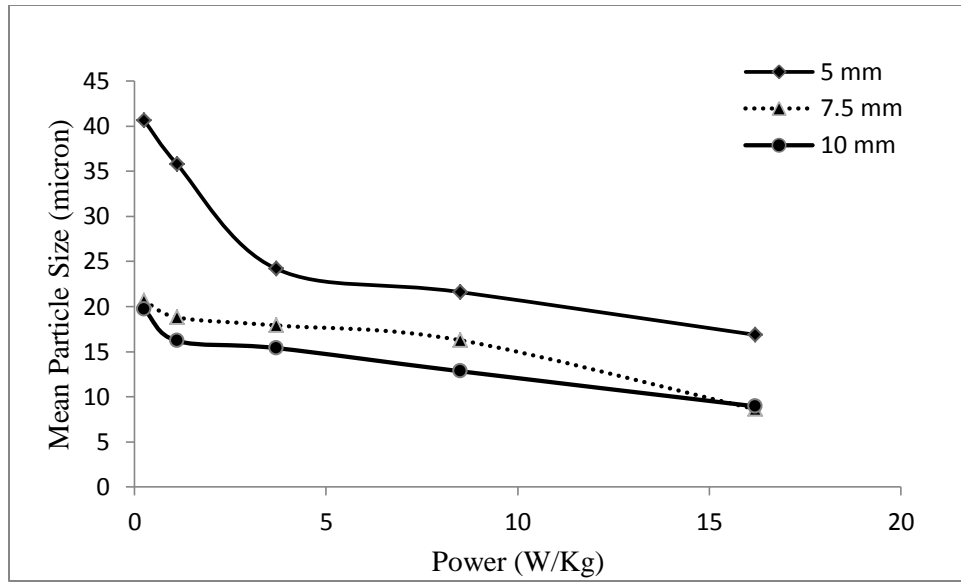


Figure 3.19 Mean particle size as a function of energy dissipation per unit mass

## **CHAPTER 4- CONCLUSION AND RECOMMENDATIONS**

The most important aspect of microencapsulation technology is to develop the process in such a way that it will not be limited to the laboratory scale and it will fulfill the process requirement. The main point is to evaluate an economical, cost effective and practically feasible implantation that is utilizable in commercial field. The microencapsulation process by dispersion polymerization has been chosen due to some advantages including low cost, high network uniformity, lack of oxygen inhibition, simplicity of the reaction, high strength, ease of modification, versatility in terms of monomers and catalysts, the ability to reach high conversion at room temperature and pressure, use of minimum number of components. The only drawback is the lack of precision of the particle. The objective of this research work is to fabricate the microparticles using a piston driven reactor and analyze the results in terms of particle size, size distribution and energy dissipation per unit mass of reactor liquid. For each reactor the assessment has been done for different stirring speed, surfactant concentration, oscillation frequency and amplitude. It has been determined that the size of the microparticles can be tuned through variations in power input into the system by means of agitation or oscillation. The oscillation amplitude has a similar effect as the oscillation frequency in controlling the particle size and size distribution. Study has illustrated that in terms of particle size, size distribution and energy dissipation, the oscillatory reactor is more preferable one than the traditional reactor with propeller.

The present work can be continued with a more extensive study of microcapsule properties and application using the oscillatory reactor so that the technology can be developed to use in the industrial level in such a way that it can satisfy all relevant product requirements including tailoring product properties, easy product handling, improved shelf life and controlled

release. A control system can be established which can detect the particle and separate them according to the size. Moreover experiment can be conducted using another type of reactor which is basically a rotary drum reactor, evaluate the performance of the reactor with respect to the other two reactors used in this research work.

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## **VITA**

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