EFFECT OF TEMPERATURE AND PROCESSING TIME ON AGGLOMERATES PREPARED BY SPHERICAL CRYSTALLIZATION

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Abstract: Spherical Crystallization process incorporates crystallization and agglomeration simultaneously in one step. In this study benzoic acid agglomerates in spherical shape are prepared using anti solvent crystallization method with methanol-water-toluene system. Here benzoic acid is dissolved in methanol to prepare a saturated solution and this solution is added to water as an anti-solvent to crystallize the benzoic acid and 3rd solvent used to collect the individual crystals and agglomerate them. Under continuous agitation, the particles become spherical shaped agglomerates due to shear force.

In this work influence of temperature on spherical agglomeration of benzoic acid was studied and observed that with increasing temperature average agglomerate size was decreased. Particle size distribution and morphology improved with increasing process time at different temperatures. The total number of particles with residence time is calculated and found that the total number of particles decreased with increasing residence time, but become denser and bigger with time.

In this work mainly solvent system has been changed and proven that it is possible to use different solvents as good solvent. kinetics has been found. Influence of temperature and processing time on Spherical crystallization of benzoic acid in Methanol - water -toluene system studied and found to have influence on the agglomerate growth. Kinetics has been found for the agglomerate growth rate and agglomeration process was described by first order kinetics.

IndexTerms - Spherical Agglomeration, Crystallization, Morphology, Particle size.

I. INTRODUCTION

Crystallization is a separation and purification technique, in which solid crystals are formed from a liquid solution. Most of the Pharmaceuticals, food and chemical industries are using the crystallization method to separate solid crystals from solution. Spherical Crystallization is a novel crystallization technique that could transform fine crystals into spherical agglomerates during crystallization. In this process as crystallization solvent three partially miscible solvents are used. The first solvent was used to dissolve the solute, second was used for crystallization and the third solvent was called a bridging liquid to promote the agglomerates formation [8, 9]. This solvent preferentially wets the crystals produced and aggregates them into agglomerated spherical form. [13,14] Gave a detailed mechanism about how the bridging liquid collects the multiple crystals by capillary forces and form an aggregate by forming liquid bridges between them then to spherical form by the action of shear force. As parameters like solute concentration, temperature, amount of bridging liquid, feed rate, processing time etc., have great impact on the spherical agglomeration many authors studied the influence of these process parameters for different compounds [1,2,7,10,11,12,14,16]. Kinetics of the spherical agglomeration has not been explained much in literature, in this work an attempt was made to explain the kinetics using number of particles formed at different temperatures and process time.

In this study experiments are conducted using benzoic acid compound (C_6H_5COOH), also called benzene carboxylic acid and phenyl carboxylic acid. It is used as a bacteriostatic, bactericidal agent and also used as preservative instead of yeast and mould [4]. Benzoic acid crystals are produced in the form of needles or flakes during crystallization. In this method, the solute is dissolved in methanol and toluene which is used as bridging liquid is added to this solution. The whole solution is added to water to produce agglomerated crystals under stirring.

II.METHODS

2.1Materials

Benzoic acid (C_6H_5COOH) 99% purity (SD Fine Chem Ltd) was used as a model drug. Methanol (99.7% purity, Rahul Chemicals) and water (filtered and de-ionized). Toluene (99% purity was purchased from Molychem).

2.2 Apparatus

250 ml jacketed crystallizer (6 cm in diameter), a three-blade marine propeller (2.5 cm in diameter) Solutions were fed by a syringe pump and the temperature was controlled by a heating and refrigerating circulation unit

2.3 Method

Approximate optimum conditions such as BSR (bridging liquid to solid volume ratio), stirring time, and concentration were taken from our previous work [15]. In a small beaker measured amount of benzoic acid is dissolved in methanol which is equal to 0.375 g/ml at 40°C. After that solution is allowed to cool to room temperature and a certain amount of toluene (BSR = 1) was added. After dissolution, at room temperature this solution can retain without crystallizing for ample time. At certain feed rate, this solution was fed into the anti solvent which is under agitation in the crystallizer. This was thermally controlled at 5, 15, and 25ºC using a heating and cooling circulator. After when the crystallization started, 5 ml of sample collected at different time intervals and filtered. The agglomerates were dried at room temperature until the weight is unchanged, after the complete drying is ensured weights (w), number (n) were measured. The total number of agglomerates N in the system is calculated by substituting total agglomerate weight W in Eqn (1) N= (W/w) n.

2.4Sieve Analysis for Particle Size Distribution (PSD)

The influence of the processing parameters on the particle size and size distribution is studied. The solid agglomerates are sieved with woven wire test sieves in the range of 0–200, 200–355, 355–600, 600–1000, 1000–1400, 1400–2000 µm fractions. Until the weight of different fractions remains unchanged the sieving was performed in 10min intervals. By measuring the weight of each sieve fractions the size distribution of the product is acquired and are furnished as cumulative over size mass distributions.

III. RESULTS AND DISCUSSION

Experimental setup used in this work is shown in Fig 1. The average diameter of spherical agglomerates at temperatures for 1 hr residence time was determined using sieve analysis. The average size of agglomerates is taken to be as 50% of the cumulative size and plotted against temperature were shown in Fig 2. The cumulative mass fraction and average diameter of the agglomerates are determined at different process times and temperatures. The size average diameters are plotted as a function of residence time at different temperatures as shown in Fig 3. At higher temperatures, the smaller agglomerates were obtained initially and with decrease in temperature the agglomerates size has increased. The average size of the agglomerates was maximum at the crystallization temperature 15ºC.

The agglomerates size distribution with residence time at different temperatures was plotted as shown in Fig 4. It was found that the agglomerates size is almost decreased with increasing crystallization temperature. The average size of the agglomerate is in the range of 1.7 to 1.95 mm at different temperatures.

The particle characteristics vary based on the sieve fraction shown in Fig 7. Very fine irregular shaped agglomerates are observed in the smallest sieve fraction 0-600 µm in size (Fig 7a and Fig 7b). Particles having sieve fraction 600-1000µm size (Fig 7c) are still irregular agglomerates in shape but seem to be dense and concentrated particles as observed under a microscope. Above particle size 1000µm, these agglomerates start to form into spherical as shown in Fig 7d and 7e. The tiny particles are thin and irregularly shaped, or fragments from larger agglomerates. The particle morphology with different times is shown in Fig 8. With increasing time particle size is increased and spherical agglomerates are formed. During the initial time, small irregular aggregates are observed in Fig 8a and 8b. After 20 mins agglomerates start to become spherical. The good spherical agglomerates are observed after 45 mins having a size 1000 µm.

Total no of agglomerates at different temperatures are plotted against the residence time as shown in Fig 5(a). Number of particles decreased with increasing residence time, but become more dense and bigger with time. The total no of agglomerates decreased rapidly at low crystallization temperature.

$$\ln N = -kt + \ln No$$

Where N and No are total number of agglomerates at residence time t and t=0 respectively, and k is constant. Particle size distribution with temperature at different times are shown in Fig 6.With increasing temperature constant k is increased, at 5ºC k value is 0.0055, at 15ºC 0.0087, at 25º C it is 0.0081. The data exhibited straight line on semi logarithmic graph as shown in Fig 5 (b), indicating that the agglomeration process was described by first order kinetics.

Discussion:

From the results it has been observed that at with decreasing crystallization temperature the size of the agglomerates has been increased. The average size of the agglomerates was maximum at the crystallization temperature 15ºC. From the literature it was found that the average size of the agglomerates was increased with increasing temperature up to 15ºC and then decreased [8]. The distribution form of the agglomerates was preserved during the spherical crystallization [5]. From the solubility curve of benzoic acid [3] and also from the work of [8] it was observed that the solubility of bridging liquid increased a little with an increase in temperature. The agglomerate size was increased with an increase in the amount of bridging liquid. So at high temperature, the amount of available bridging liquid was increased, resulting yield of large agglomerates. It was reported from previous investigations that fine particles are needed a small amount of bridging liquid to produce larger agglomerates than coarser particles since the adhesive force between fine particles and bridging liquid is stronger than coarser particles and bridging liquid [14]. At low temperature, the recovery of crystals increased and crystal size decreased [6]. A reason for this is that ‘’the lower solubility at a lower temperature will lead to a higher supersaturation, and this should lead to stronger nucleation and smaller product crystals’’. It was assumed that amount of bridging liquid which is available is sufficient for agglomeration of small particles to obtain bigger agglomerates.

The particle characteristics vary based on the sieve fraction very fine irregular shaped agglomerates are grown to bigger agglomerates. With increasing processing time particle size is increased and spherical agglomerates are formed in due course of time. Particle size increases with processing time due to continuous agitation of slurry and it leads to a gradual consolidation of the agglomerates, reducing the size and porosity of the particles. This causes the bridging liquid rich solution is squeezed out to the particle surface and may contribute to further growth by coalescence with other agglomerates/crystals [13]. Hydrodynamics are responsible for bringing particles together for the agglomeration. The shear forces of the agitated liquid, collisions with surface of equipment and other particles are kneading and shaping the irregular agglomerates into almost perfect spherical shaped agglomerates.

Conclusions:

Spherical agglomerates of benzoic acid with the solvent system methanol - water- toluene has been successfully prepared. With decreasing temperature the agglomerate size increased upto 15ºC. With increasing processing time the small crystals, agglomerated and become more spherical during the course of time under the agitation. Agglomeration process was described by first order kinetics.

List of Abbreviations: Not Applicable

Figs:

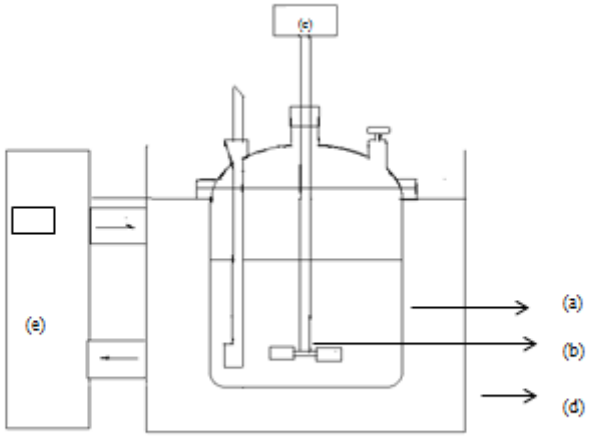


Fig 1 Experimental set up for Spherical Crystallization of Benzoic Acid. a. Crystallizer, b. Agitator, c. Agitating Control Unit, d. Heating and Cooling Circulator e. Regulator

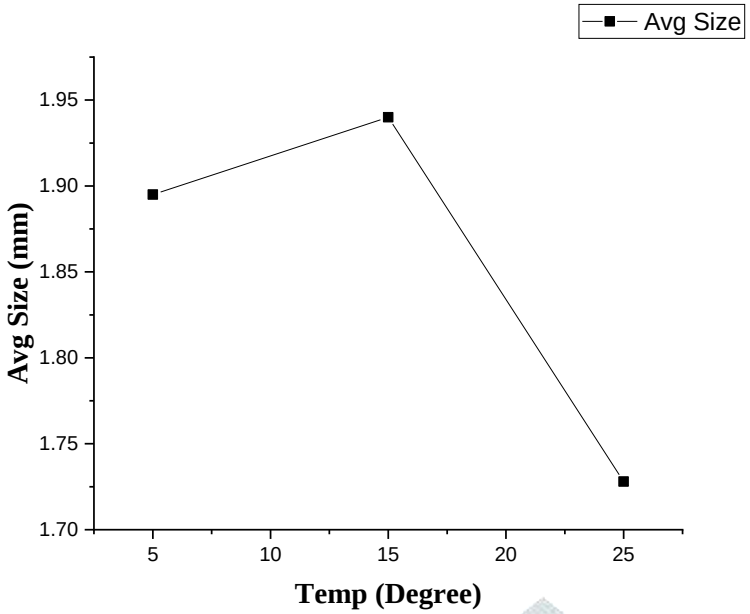


Fig 2. Effect of temperature on the average diameter of agglomerates, Benzoic acid conc. = 0.375 g/ml, N=600rpm, BSR=1

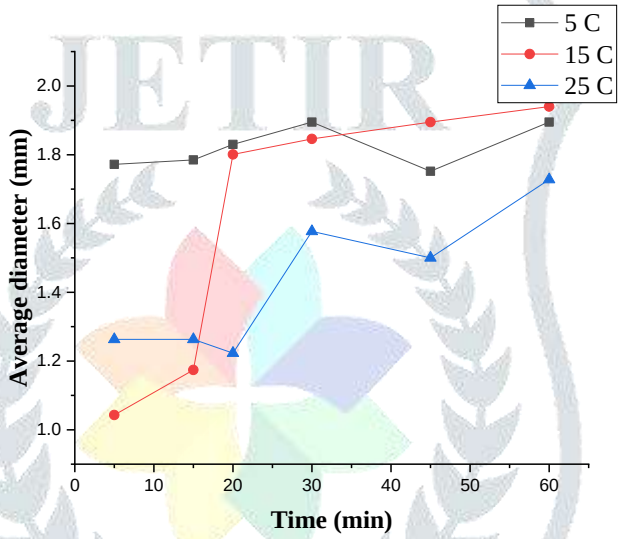
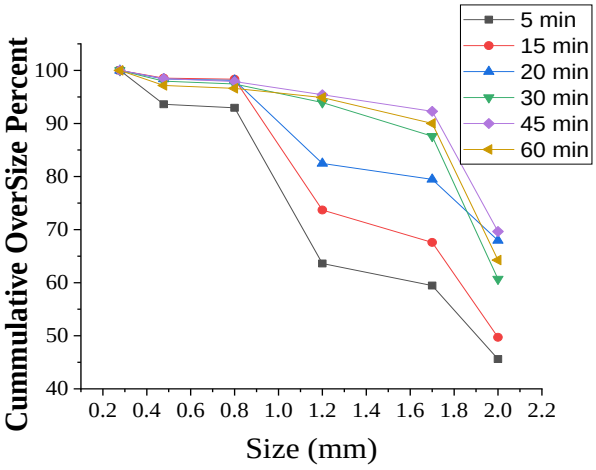
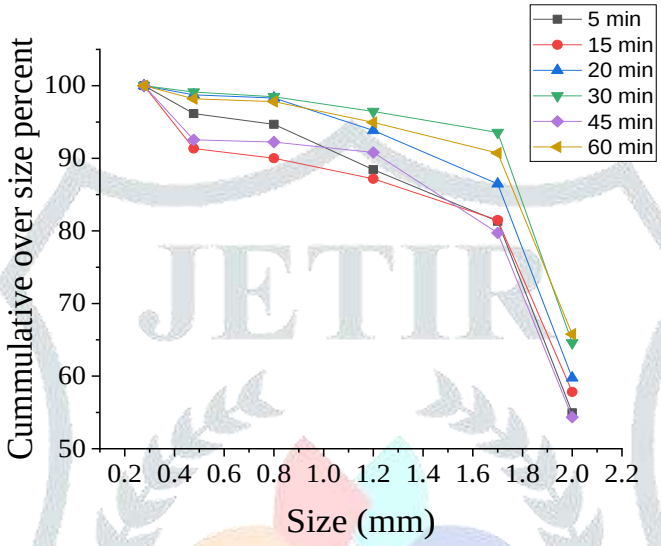


Fig 3. Average diameter of agglomerates as function of residence at different temperatures time, Benzoic acid conc. = 0.375 g/ml, N=600rpm, BSR= 1.

a)



b)



C)

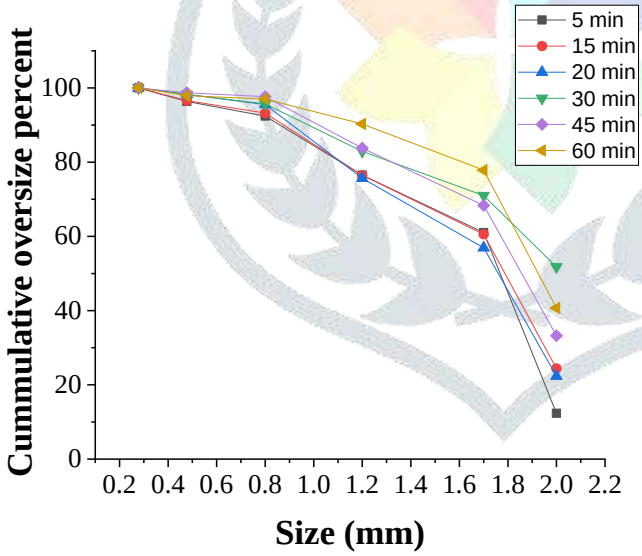
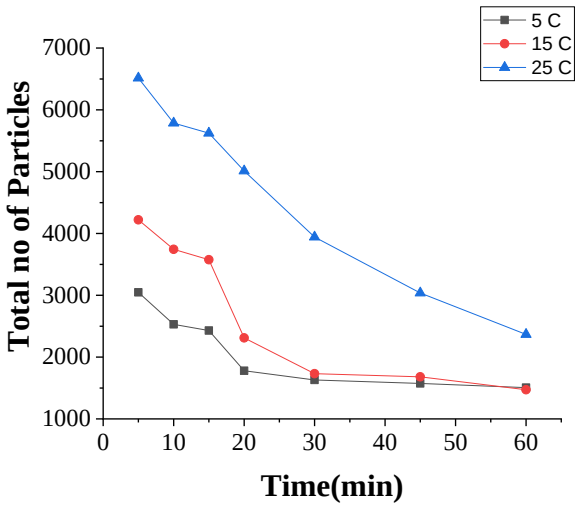


Fig 4. Size distribution of agglomerates. Agglomeration temperature a) 5ºC b) 15ºC c) 25ºC, , Benzoic acid conc. = 0.375 g/ml, N=600rpm,BSR=1

a)



b)

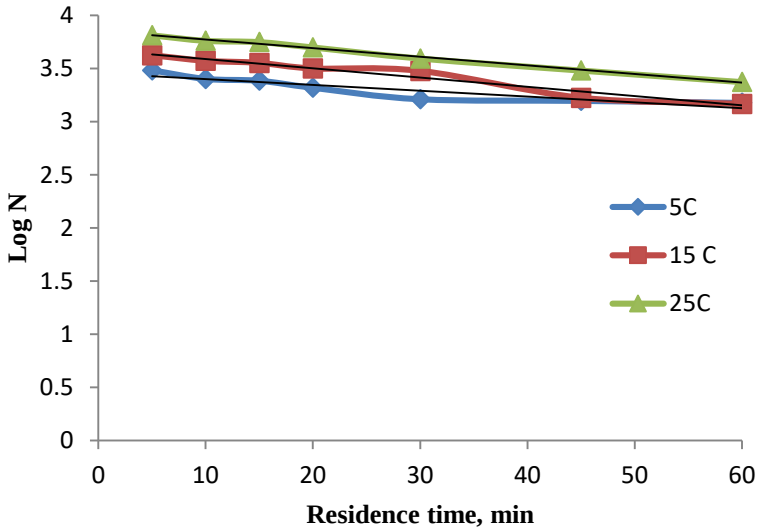
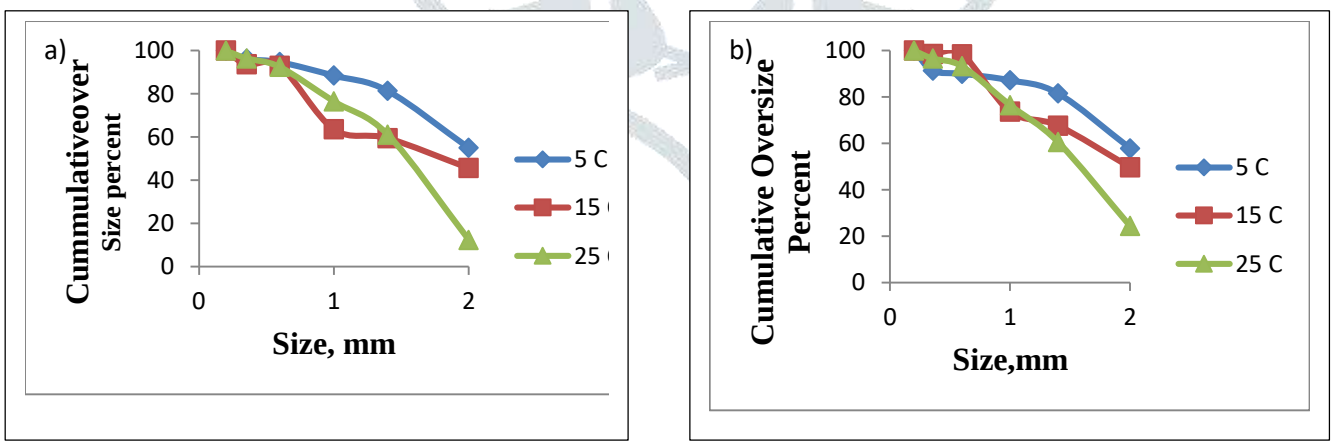


Fig 5. No of agglomerates n as a function of residence time at different temperatures a) n verses residence time b) log n versus residence time, , benzoic acid conc. = 0.375 g/ml, n=600rpm, bsr=1



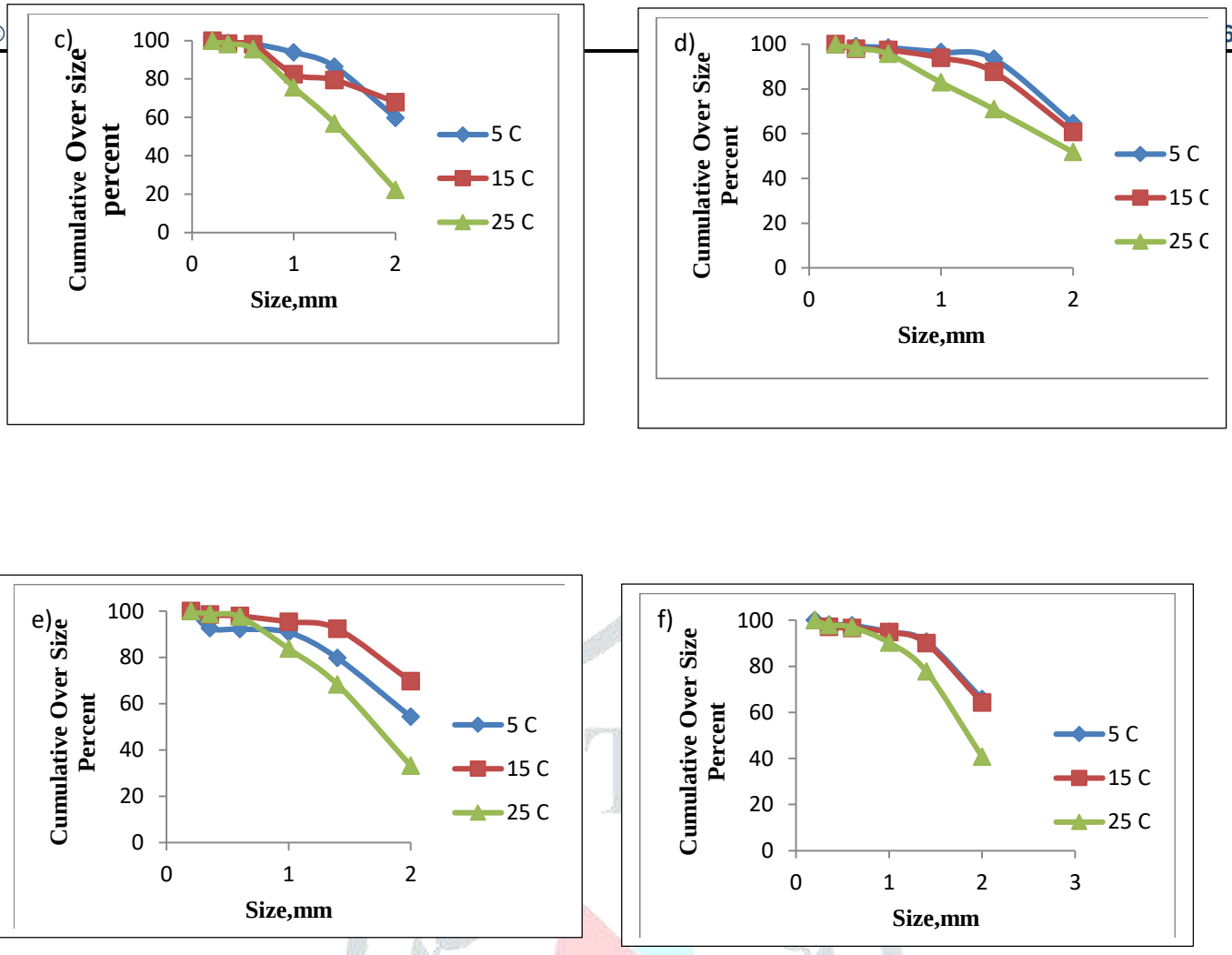


Fig.6: Change in particle size distribution with temp at different times, Benzoic acid conc. = 0.375 g/ml, N=600rpm, BSR=1. a)5 min b)15 min c)20 min d)30 min e) 45 min f) 60 min

Fig.7. Particle morphology of different sieve fractions (a) 0-355 µm (b) 355-600µm (c) 600-1000µm (d) 1000-1400 µm and (e) 1400-2000µm. Benzoic acid conc. = 0.375 g/ml, N=600rpm, BSR=1, Time at 45 min

Figure 8: Particle morphology at different times (a) 5min (b)10 min (c) 20 min(d) 45 min (e) 60 min Benzoic acid conc. = 0.375 g/ml, N=600rpm, BSR=1, size= 1 mm

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