Chapter I

General Background

Introduction

Spray drying is a useful method for the processing of pharmaceuticals since a number of formulation can be accomplished in a single step in a spray dryer. This can both simplify the process and shorten the processing time. In addition, it offers a means for obtaining powders with predetermined properties such as particle size and shape (Broadhead et al, 1992). Spray drying has a wide range of applications within pharmaceutical industries including drying of heat sensitive material (Masters, 1979; Labrude et al, 1989), improving solubility of poorly water soluble substances (Tsuda et al, 1988; Corrigan and Hollohan, 1984; Corrigan et al, 1984), preparing direct compression vehicles (Raff et al, 1961) and coating drugs with suitable polymers to produce dust-free powder (Seagar, 1977).

Recently, there has been a renewed interest in the use of spray drying to modify the release characteristics of the pharmaceutical products (Bodmeier and Chang, 1988; Takeuchi et al, 1987; Wan et al, 1990;

Takeuchi et al, 1989; Kawashima et al, 1972; Leesawat, 1991; Wan et al, 1992). This technique is useful because microspheres can be prepared directly from droplets in a single process.

An ambitious shift has been made from the use of organic system to the use of aqueous system because of avoiding explosion hazard and toxicity associated with solvent system. Takeuchi, Handa and Kawashima (1989) reported the preparation of the controlled release theophylline tablets with acrylic polymer in a compress system by using spray drying technique in aqueous system. The controlled drug release was attributed to continuous and well-dispersed polymer matrix formed by spray drying and subsequent compressing process. Leesawat (1991) prepared controlled release theophylline matrices with cellulose polymer in aqueous system by spray drying technique. It was found that 300 mg-theophylline matrices containing 3% ethylcellulose and 25% lactose exhibited satisfactory controlled drug release. Although there are a number of reports on the use of spray drying in producing controlled drug release system, no much attention has been paid on the investigation of the processing techniques in preparing controlled release matrices. This work was the expansion of the study reported by Leesawat (1991) in investigating the effects of processing variables on the physical properties of spray dried powders and release

characteristics of matrices prepared. The processing variables included in this investigation were the inlet air temperature, the feed rate of the spray drying solution, the atomizing air pressure and the concentration of feed solution.

In addition, the tabletting characteristics of the spray dried powders produced was also studied. The suitability of spray drying technique in the manufacture of controlled drug release matrix was investigated, especially the reproducibility of the drug release pattern from the matrices prepared from consecutive batches as well as when the batch size was increased. The variation of the drug release pattern within batch of the spray dried matrices and two commercial products (Theodur $^{(R)}$, Nuelin $^{(R)}$) were comparatively studied.

Objectives of the Study

1. To study the spray drying technique in the preparation of co-spray dried matrices of theophylline-ethylcellulose-lactose.

2. To study the effect of processing variables on physical properties of spray-dried powders and drug release pattern of resultant matrices.

3. To study the effect of compressional pressure during tabletting on the release of drug from matrices.

4. To study the reproducibility of drug release pattern in consecutive batches and drug release pattern of spray-dried matrices within batch.

5. To explore this lab-scale data as a guide for developing theophylline controlled release matrices on a production scale.

Literature Review

1. Spray Drying Technique

Spray drying techniques have been widely used in the pharmaceutical, chemical and food industries. Its main uses in the pharmaceutical industries include drying of heat-sensitive materials, improving solubility of poorly water soluble substances (Tsuda et al, 1988; Corrigan and Hollohan, 1984; Corrigan 1984), preparing granulations for tabletting (Raff et al, 1961) and coating drugs with suitable polymers to produce dust free powders (Seagar, 1977) and also to produce controlled release products (Takeuchi et al, 1989; Leesawat, 1991).

The following topics provide a brief overview of the design and operation of spray dryer, the effects of processing variables on particle properties, the application of spray drying technique in controlled drug release systems and the production of granulation by spray drying technique.

1.1 The Design and Operation of Spray Dryers

Spray drying converts a liquid into a powder in a one step process. It is capable of producing fine, dustless or agglomerated powders to precise specifications. The spray drying process encompasses the following four stages (Nielson,1982):

(i) Atomization of the feed into a spray

(ii) Spray-air contact

(iii) Drying of the spray

(iv) Separation of the dried product from the drying gas

There are a variety of atomization systems available, which may be classified according to the nozzle design as rotary atomization, pressure atomization or two-fluid (pneumatic) atomization. In rotary atomization the feed fluid is introduced into the drying chamber by means of a spinning disc or wheel which created a spray of droplets. Pressure atomization, as the name suggested, occurs when the feed is fed to the nozzle under pressure which causes the fluid to be dispersed into droplets as it leaves the nozzle. Finally, in two-fluid nozzle, the feed fluid and atomizing air are passed separately to the nozzle where they mix and the air causes the feed to break up into a spray. Two-fluid nozzles are generally confined to laboratory scale spray dryers (such as the Buchi 190 which is commonly used in pharmaceutical research).

Examples of handy, small-size spray dryers having a drying chamber of a diameter of about 1 m. are listed below. (Kondo,1979)

-Niro (minor unit): centrifugal type provided with air turbine (Denmark)

-Bowen (Laboratory use): centrifugal type driven by motor(USA)

-Swenson (Laboratory use): two-fluid nozzle type (USA)

-Lurugi (Model 10): centrifugal type driven by motor (West Germany)

Spray dryers may be designed to operate in a co-current manner, where spray and drying air pass through the dryer in the same direction or in a counter-current manner where the spray and drying air enter the drying chamber at opposite ends. Other spray dryer designs are available where the spray-air contact is intermediate between co- and counter-current. Co-current operation is preferable for the drying of heat sensitive materials since the dry product is in contact with only the coolest air. Also, the high rates of moisture evaporation enable the temperature of the dry product to be considerably lower than that of the air leaving the drying chamber. Counter-current drying, on the other hand, is a superior process in terms of heat utilization and economics, but subjects the driest powders to the hottest air stream.

The final step in the spray drying process involves the separation of the product from the air stream. This is usually accomplished by means of a cyclone separator through which the air and product pass after exiting the drying chamber. Many dryers also allow for product

collection at the base of the drying chamber.

There are numerous different spray dryer designs. Spray dryers system are usually open cycle whereby the drying gas is discharged after use. For dryers operating in this manner, the drying gas would usually be air. In addition, however, closed cycle spray dryers are available which enable organic solvents to be used as the feed medium. In this type of dryer, the drying air is replaced by an inert gas, usually nitrogen, which is continuously recirculated. The organic solvent is also recovered. Other dryers are available which operate using air with a reduced oxygen content. This may be required if the material being dried is extremely susceptible to oxidation or has explosive tendencies (Nielson, 1982). Various dryer layouts suitable for toxic materials which operate so as to avoid air pollution have also been developed. From a pharmaceutical point of view, it is important to note that aseptic systems are available which operate to produce a sterile powder. This is achieved by filtration of the liquid feed material and the atomizing air, contamination free atomization and product collection, and careful dryer design. These systems are currently used for the production of antibiotics. Also, dryers which incorporate fluid beds into the base of the drying chamber have been designed. These are capable of producing large agglomerated powders more economically than other types of spray dryer.

The main disadvantage of spray drying for many applications is its cost, in terms of both equipment and operation. Spray dryers have poor thermal efficiency unless extremely high drying temperature are used. This is impossible for the majority of products, including pharmaceuticals, because of the heat degradation which would result. For many pharmaceuticals, however, the cost of the end product may be sufficiently high that the use of spray drying is both feasible and desirable. Thus the expense of the process must be balanced against the advantages to be gained by using spray drying instead of an alternative processing strategy, and the value of the end product (Broadhead et al,1992).

1.2 The Effects of Processing Variables on Particle Properties

Spray dried powders are usually approximately spherical with a narrow size distribution and are usually hollow. The hollow nature imparts a low bulk density to the powders, but despite this, their spherical shape means that they are usually free-flowing. By modifying the spray drying process, it is possible to alter and control the following properties of spray dried powders; appearance, particle size and size distribution, bulk density, particle density, porosity, moisture content, flowability, stability, dispersability, friability and retention of activity, aroma and flavor (Newton,1966).

An increase in the energy available for atomization (i.e. rotary atomizer speed, nozzle pressure, or air-liquid flow ratio in a pneumatic atomizer) will reduce particle size (Masters,1979). Particle size is usually increased as the feed concentration or viscosity increases. Masters reported that surface tension has a minimal effect on particle size, although Kata and Wayer (1985) reported an increase in particle size with an increase in feed surface tension and density as well as with concentration and viscosity. If the feed rate is increased, particle size will again increase. The effect of temperature on particle size appears to be highly dependent on the material being dried (Crosby and Marshall, 1958). It was observed that for crystalline materials, such as sodium sulfate, temperature had very little effect whereas for coffee extract (a film forming material) the mean particle diameter was significantly reduced by increasing the inlet air temperature. In contrast, Newton (1966) reported a study where the particle size of some materials was shown to increase as the drying air temperature increased. High drying air temperature also seem to be associated with lower bulk densities (Masters,1979). As a general rule, smaller particles will usually be more dense, and so the bulk density of a powder with a small particle size will be higher. Bulk density will also increase with a narrower particle size distribution (Newton,1966). As it would be expected, increased dryer outlet temperatures result in a

lower final product moisture content.

The spray congealing had been use for production of sulfaethylthiadiazole(SETD)-hydrogenated castor oil granules (Robinson and Swintosky, 1959). A decrease in particle size was observed with a decrease in nozzle diameter, as it would be expected. The type of wax used also had a significant effect on particle size. Interestingly, these authors observed larger particle diameters with the least viscous feed solutions. This corresponded with the data of Scott et al. (1964), who observed an inverse relationship between particle size and the viscosity of the feed medium, but contrasted with most other observations of the spray drying process which indicated an increase in particle size with increasing feed viscosity. In addition, Scott et al.(1964) also reported that the mean surface volume diameter was found to increase with decreasing wheel speed and increasing feed rate. Variation in wheel speed was more important in controlling particle size than variation in feed rate, whereas viscosity of the feed, had relatively little influence.

2. The Applications of Spray Drying Technique in Controlled Drug Release System

Spray drying is not a new technology as far as the pharmaceutical industry is concerned, having been used successfully since the early 1940's. It is a useful method

for the processing of pharmaceuticals since it offers a means for obtaining powders with predetermined properties, such as particle size and shape.

There has been a renewed interest in the use of spray drying to coat drugs with polymers to produce dust-free controlled release product. The advantage of using this technique over other coating methods is that the coated particle can be prepared directly from droplets in a single process. Moreover spray-dried products are also known to have improved flow properties, thus increasing the ease of incorporation into a dosage form.

Microcapsule can be either an individually coated solid particle or liquid droplet, or matrix of wall material containing many small, fine core particles. The former type of microcapsule can be prepared by numerous methods including coacervation, coating and interfacial reaction techniques. Matrix microcapsules are usually prepared by spray drying or spray congealing. Spray drying can be used simply to separate previously prepared microcapsules from the vehicle, or for the preparation of microcapsules in a single operation (Voellmy et al. 1977). In the spray congealing process, no solvent is used. The feed, which consists of the coating and core materials, is fed to atomizer in the molten state. Microcapsules form when the droplets meet the cool air in drying chamber and congeal (Deasy,1984).

Biodegradable microcapsules have been prepared by spray drying. Polylactic acid (PLA) microcapsules were prepared from solutions or suspensions of a number of drugs dissolved or dispersed in methylene chloride (Bodmeier and Chen, 1988). Microcapsules of progesterone-PLA were formed with diameters of less than 5 μm. The microcapsules became more spherical as the progesterone content was increased. Crystallization occurred in the aqueous phase when the microspheres were prepared by a solvent evaporation method, but spray drying avoided this problem. The major difficulty encountered in preparing the spray dried microcapsules was the formation of polymer fibers as a result of inadequate forces to disperse the filaments into droplets; the successful atomization into droplets was dependent on both the type of polymer used and, to a lesser extent, the viscosity of the spray solution.

Wise et al. (1976) prepared biodegradable microcapsules of a lactic-glycolic acid copolymer by spray drying. The core material was an antimalarial drug. The microcapsules were subsequently suspended in carboxy methylcellulose and injected into rats for evaluation as an implantable drug delivery system.

Takenaka et al. (1980) prepared enteric coated microcapsules of sulphamethoxazole by spray drying an aqueous solution of drug and cellulose acetate phthalate (5%), with or without various additives, such as

monmorillonite clay and colloidal silica. A new in vitro release simulator to study the drug release from encapsulated tablets in the GI tract was devised. Particles with diameters ranging from 3.6 to 22.0 μm were obtained. Formulations containing additives yielded smaller particles than those without additives. The addition of additives also improved the surface texture of the spray dried products, as compared to particles prepared from non-additive formulations, which tended to have flaky surfaces. Non-additive formulations also exhibited poor flow properties and thus were not easily tableted, whereas formulations which included additives were tableted easily. All sulphamethoxazole formulations containing cellulose acetate phthalate (CAP) exhibited some conversion of the drug from crystalline form I to form II and an amorphous form during spray drying (Takenaka et al., 1981). Form II was also obtained by freeze drying or vacuum drying sulphamethoxazole. When microcapsules were prepared by a coacervation technique the drug remained in form I. CAP was presumed to interact with the sulphamethoxazole, since the degree of amorphism increased with an increase in the concentration of CAP in the formulation.

Further studies examined the effect of spray drying sulphamethoxazole with xanthan gum or guar gum, with and without colloidal silica or cellulose acetate phthalate (Kawashima et al. 1983). It was found that the film forming capacity of xanthan gum alone was superior to that of guar

gum, but inclusion of colloidal silica or cellulose acetate phthalate made the resultant product smoother still. X-ray diffraction data showed that the presence of cellulose acetate phthalate actually caused a polymorphic change resulting in a mixture of forms I, II and III (form III had been indistinguishable in the previous study which used IR analysis). When the formulation contained colloidal silica, however, the sulphamethoxazole was always present in form I, irrespective of the gum type. When either CAP or colloidal silica was included in the formulation, the product was usually a mixture of all three forms.

An alternative technique for the preparation of microcapsules in a spray dryer was that of spray polycondensation (Voellmy et al. 1977). This was a technique whereby polymer formation formed reactive monomers, encapsulation and product separation from the vehicle were all accomplished in a one stage process. The feed consisted of a dispersion of the core material and monomers, or precondensates of relatively low molecular weight, in addition to other film forming agents and the catalyst. This technique was used by Voellmy et al. (1977) to produce microcapsules which developed slow release properties after curing.

Gidwani et al. (1992) prepared spray dried enteric solid dispersion of a pentapeptide analog of thymopentin (IRI-426). IRI-426 (Ac-Arg-Pro-Asp-Val-Phe-NH_2)

018776

is a biologically active and enzyme-resistant analog of thymopentin (Arg-Lys-Asp-Val-Tys), a pentapeptide corresponding to an active site of the thymic hormone thymopoietin. Enteric formulation of this enzyme resistant pentapeptide could be valuable for oral administration by providing protection from acid proteolysis in the gastric juice and release and absorption in the duodenum. A solid dispersion of IRI-426 coated by spray drying with a pH-sensitive polymer Eudragit S-100 in the drug-to-polymer ratio of 1 to 10 exhibited rapid release at pH 7 and slow release at pH 1.2. Compaction of the spray-dried enteric solid dispersion powder or enteric coating of the capsules filled with the spray-dried enteric solid dispersion powder caused retardation of drug release at pH 1.2 as well as pH 7. Spray dried enteric coated solid dispersion powder in uncoated gelatin capsules appeared to be the best formulation to deliver this peptide to the upper small intestine.

Lin and Kao (1991) prepared sodium diclofenac-coated microcapsule by a spray drying technique with Eudragit L30D as enteric-coating material. The spray dried powder, mixed with Neocel or Flo-starch, or the mixture of Neocel and Flo-starch (weight ratio, 1:1) was directly compressed into a tablet. The spray dried powder, the mixed powder before tabletting, and the tablets all exhibited enteric-coated release properties. The weight ratio of Neocel to Flo-starch plays an important role in controlling

the release of sodium diclofenac from enteric tablets. The 1:1 weight ratio of Neocel to Flo-starch was more suitable for designing the microdispersed sodium diclofenac enteric coated tablets.

Wan et al. (1990) studied influence of operation and formulation factors on spray-dried microcapsules of theophylline using aqueous solution of hydroxypropylmethylcellulose (HPMC) as the coating polymer. The operation variables found to affect product properties significantly were the nozzle size and temperature. The flow properties of products improved with an increase in nozzle size or a decrease in the air/liquid diameter ratio, an increase in inlet temperature and a decrease drug polymer ratio. There was reduction in drug dissolution rate with increasing in temperature. The type of feed used was important, a suspension feed resulted in a more sustained release and better flow properties than a solution feed. Drug polymer ratio showed an unusual trend in the drug release profiles were discussed. The authors reported further study about the effect of different coating polymer by spray drying process (Wan et al. 1992). Various polymers; hydroxypropylmethylcellulose acetate succinate (HPMCAS), hydroxypropylmethylcellulose (HPMC), methylcellulose (MC) and sodium carboxymethylcellulose (NaCMC) were evaluated for their spray-coating properties. The drug release from the coated products was dependent on

the hydrophilicity of the polymer. NaCMC, which was more hydrophilic, gelled faster and retarded the drug release more effectively. HPMC and MC produced products with similar dissolution profiles and flow properties. Spray coating with HPMCAS was unsuccessful. The polymer also affected the size and cohesiveness of the products.

Spray drying had frequently been used for the production of slow release granulations. Kornblum (1969) reported that significantly less binder was required to achieve a given sustaining effect when compared with conventional granulation methods.

Kawashima and Takenaka, (1974) prepared slow release magnesium carbonate granulation by spray drying. They observed that the degrees of drug release retardation afforded by the binder seemed to be associated with the degree to which the binder encapsulated the magnesium carbonate.

Controlled release theophylline tablets were prepared by compressing spray dried microspheres containing Eudragit L30D, L100-55 and E30D (Takeuchi et al. 1989). Depending on the amount of polymer present, the spray dried powder consisted of either agglomerated, polymer coated theophylline crystals or spherical particles of a solid dispersion of amorphous drug in a polymer base. Completely enteric function was observed with drug-to-polymer ratio of

1:3 using Eudragit L30D or L100-55. Tablet with Eudragit E30D formulated at 2-40% level showed good sustained drug release which was thoroughly independent of the pH of dissolution media. In each tablet, the controlled drug release was attributed to continuous and well-dispersed polymer matrix formed by spray drying and subsequent compressing process.

Controlled release theophylline matrices containing cellulose derivative (ethylcellulose, hydroxypropylmethylcellulose, hydroxypropylmethylcellulose phthalate) were also prepared by spray drying technique (Leesawat, 1991 ; Kulvanich and Leesawat, 1991). The types and amounts of matrix additives affected the physical properties of co-spray dried powders. The matrix of theophylline 300 mg. with 3% ethylcellulose and 25% lactose exhibited the most satisfactory release profiles.

Asker and Becker (1966) used spray drying technology to produce prolonged release sulfaethylthiadiazole (SETD) granulations. A follow-up series of papers investigated the production of slow release sulphaethylthiadiazole-wax granulations by spray congealing (Cusimano and Becker, 1968; John and Becker, 1968; Hamid and Becker, 1970). In a series of papers by John and Becker;and Cusimano and Becker, certain details of spray congealing process for SETD were investigated, such as the composition of the coating wax, the nozzle size of the atomizer, and the

presence of surfactant in the wax matrix. Both decreasing nozzle size and increasing surfactant concentration tended to produce products with a faster rate of drug release in acid pepsin or alkaline pancreatin media. However, dissolution behavior was most affected by the type of waxy coating material used. White beeswax, glyceryl tristearate, carnauba wax, hydrogenated castor oil, cetyl alcohol, and glyceryl monostearate were examined. In subsequent paper by Hamid and Becker, the in vitro dissolution patterns of some spray-congealed SETD wax products in tablets form were studied. Tabletting caused a decrease in the rate of drug release. This technique had previously been used for the production of 35 μm SETD-hydrogenated castor oil granules, which were used in the formulation of a slow release suspension (Robinson and Swintosky, 1959). The researcher prepared particle of SETD by mixing them with molten hydrogenated castor oil at 110°C; the suspension was then spray congealed into an air-cooled chamber using a centrifugal wheel atomizer. The spherical microcapsules obtained were observed to consist of finely divided drug particles uniformly dispersed throughout a matrix of hydrogenated castor oil and to have a uniform film of the oil over the surface of each microcapsule.

Scott et al. (1964) reported that waxes, fatty acids or alcohols, sugars and other coating materials that melt without decomposition at high temperature and solidify at normal storage temperature were suitable for spray

congealing. They used molten stearic acid thickened with dissolved ethylcellulose at 70°C without any core substance in a modified Laboratory Niro spray dryer fitted with a centrifugal wheel atomizer and having an ambient air inlet temperature of 25 to 27°C. The particle size of spray-congealed coating material was 17 to 40 μm for mean surface volume diameter.

3. The Production of Granulation by Spray Drying Technique.

Spray drying is useful alternative to wet granulation for tablet formulations that cannot be directly compressed. Slurries of up to 60% solid can be dried successfully (Newton, 1966).

Raff et al. (1961) described the production of a spray dried granulation from a slurry of approximately 50-60% solids by weight, composed of filler, binder, disintegrant and a coloring agent if desired. The granulation could then theoretically be mixed with up to 90% medicament prior to compression, although in the case described the drug (chlorpromazine) was present at a concentration of less than 3%. Particle size ranges of 10-70 μm were obtained using a laboratory scale spray dryer but a size range of 100-250 μm was found to be most advantageous for tablet preparation on a large scale. The advantages of this method of granulation over traditional methods were reported to be; improved flowability, improved color

uniformity, improved stability, improved hardness and lower lubricant requirements.

Spray drying was used to agglomerate aluminum silicate and magnesium carbonate with various binders, in order to improve flow and other tabletting properties (Takenaka et al. 1971). The granules produced had diameters of 10-80 μm as compared to 1-8 μm for original samples and were free flowing in almost all cases. The geometric mean diameter was found to be most dependent on the type of binder used, and also the binder concentration. The smallest particles resulted from the binder free formulations. The granules containing binder could all be tableted easily which the original powders could not. Formulations with higher binder concentrations had improved flow properties and resulted in tablets with the highest apparent density and hardness.

Cham et al.(1987) compared conventional granulation with spray drying for the production of heavy magnesium carbonate powder. They found, however, that conventional granulation imparted better flow properties and a higher bulk density than spray drying. They attributed these results to the regular particle shape achieved by conventional wet granulation. This contrasted with observations by other authors that spray drying produces regularly shaped spherical particles with good flow properties.

Sugimori et al. (1990) compared high speed mixing, fluidized bed granulation and spray drying in the production of acetaminophen and ascorbic acid granules. In both cases, spray drying produced the smallest granules. The tensile strength of tablets produced from the different types of granules was found to be more dependent on the amount of water used in granulation than on the granulation method. The authors pointed out, however, that spray drying is a useful method for mass production of granules, since it makes continuous granulation possible.

Seager et al. (1979) and Rue et al. (1980) compared the structure and tabletting properties of acetaminophen granules produced by spray drying, roller compaction and wet massing, using gelatin as a binder. They observed that in spray dried granules the binder concentrated as a shell at the surface of the spherical granules. By comparison, in wet massed granules the binder was distributed through the agglomerates in a sponge like matrix, and in roller compacted granules the binder was present as discrete particles embedded in the agglomerates.

At any given compaction pressure, the strongest tablets were produced from spray dried granules. This phenomenon was attributed to the concentration of the binder at the granules surface where it was ideally placed to form inter-granular bonds. As the binder concentration in the spray dried granules increased from 1% to 3%, tablet

strength also increased, but above this, tablet strength was not influenced by binder concentration. The low tablet strengths observed at low binder concentrations was attributed to the presence of incomplete gelatin shells around the granule. Once the binder shells were continuous, however, the area of inter-granular bonding became constant and hence tablet strength also reached a plateau.

4. Ethylcellulose

Ethylcellulose has long been used for coating tablets, granules and powders, but it is insoluble in water and therefore must be used with organic solvents. The water-based film-forming dispersion of ethylcellulose are available that avoid the problems of solvent-based systems. Surelease(R) is one of these products. Surelease(R) is a completely plasticized aqueous polymeric dispersion that consists of ethylcellulose in ammoniated water and is prepared by phase inversion (Chang, Hsiao, and Robinson, 1987 ; Klinger et al, 1990). The product is a milky liquid in which dibutyl sebacate and oleic acid are incorporated within the dispersed polymeric system during the manufacturing process. Ammoniated water is used to help stabilize the dispersed polymer. In addition, the dispersion contains fumed silica which acts as an antiadherent and facilitated the application of Surelease(R) during the coating process. The total solid content of Surelease(R) is 25% , 70% of which is ethylcellulose. In

conclusion, 100 g of Surelease(R) has 17.5 g of ethylcellulose.

Ethylcellulose is the ethylether of cellulose and can contain 44.0 and 51.0 percent of ethoxy groups. Ethylcellulose is resistant to alkali, both dilute and concentrated, and also to salt solutions. It can withstand dilute acids for a limited period of exposure. It is subject to oxidative degradation in the present of sunlight or UV light at elevated temperatures. Ethylcellulose is incompatible with paraffin wax and microcrystalline wax. It is presented as a non-toxic substance.

5. Advantages of Spray Drying (Masters, 1979; Mcketta, 1983)

5.1 Spray drying is a single-step operation from liquid feed to dry product. Frequently this eliminates such steps as precipitating or crystallizing, centrifuging or filtering, grinding, classifying, and perhaps the additional pumping, storage, and dust collecting operations associated with them.

5.2 The process is continuous, although it can operate with feed from a prior batch process.

5.3 Adaptable to full automatic control.

5.4 Dried product specifications meet through dryer design and operational flexibility:

5.4.1 Required product form (particle as spheres, fines, agglomerates)

5.4.2 Required properties (dusty or dustless, degree of flowability, wettability, etc.)

5.5 Applicable to both heat sensitive and heat-resistance materials.

5.6 Feedstocks in solution, slurry, thixotropic paste or melt form can be handled, if pumpable.

5.7 Corrosive and abrasive feed stocks can be readily handled.

5.8 Corrosion is reduced or prevented because the material does not contact the equipment surfaces until it is dry. This permits selection of lower-cost materials of construction.

5.9 Maintenance costs are low because there are few moving parts.

5.10 Labor costs are low because only one operator is required, even on large installations. Because the evaporation usually is done under slight vacuum, it is easy to keep the equipment and area clean.

5.11 Operator requirements are the same for both small and large dryers, hence spray drying is basically a high-volume system with low labor cost.

5.12 In co-current designs, surface temperatures are low (except at the hot gas inlet) because the extremely rapid evaporation cools the inlet gas nearly to its outlet temperature a few inches from the points of

atomization. This feature further restrains corrosion of the equipment.

5.13 Spray drying is an airborne process, hence there is very low material holdup in the equipment.

5.14 Designs are available to handle:

5.14.1 Evaporation of organic solvents without explosion/fire risks.

5.14.2 Powders that form potentially explosive mixtures in air.

5.14.3 Products that create odor during drying.

5.14.4 Toxic products.

5.14.5 Products requiring aseptic/ hygienic drying conditions.