CHAPTER IV

DISCUSSION AND CONCLUSIONS

Identification of the Spray Dried Products

Spectrophotometric analysis by an infrared spectrophotometer, powder X-ray analysis by a diffractrometer, and thermal analysis by a differential scanning calorimeter of the microparticles were conducted to physicochemically identify the crystals of diclofenac sodium were encapsulated by the polymers.

IR spectra of the spray dried products, diclofenac sodium with different the polymers (HPMC, ethylcellulose and chitosan) at various types and proportions of polymer in the formulations, showed a broad peak of polymer contained in the product at 1000-1200 cm. $^{-1}$ that partly impaired the identification of the spray dried products. The characteristic bands of diclofenac sodium appeared at 756, 775, 1286, 1308, 1504 and 1572 cm.$^{-1}$, strongly suggesting the existence of diclofenac sodium in the products.

X-ray diffraction patterns of the spray dried products, diclofenac sodium with ethylcellulose has shown that the drug present was in crystalline form. Although the intensity of X-ray diffraction peak of the product was weaker than that of diclofenac sodium, the characteristic peak of diclofenac sodium at the diffraction angles 6.5°, 8.5° and 11° were detected. For the spray dried product with HPMC exhibited no diffraction peak, but instead displayed a halo pattern, indicating that the spray dried diclofenac sodium was amorphous. In the case of the spray dried products with chitosan, HPMC with

ethylcellulose and HPMC with chitosan, the reduced intensities of the product peaks indicated that some crystals in the product converted to a disordered form due to rapid crystallization during spray drying. Takeuchi et al. (1989) suggested that the polymer to drug ratio was an important factor for formulation of the amorphous state in the system. The transformation into amorphism was not complete because a part of drug remained undissolved in the fed fluid. Most drugs were crystallized without amorphism in the spray dried particles when the polymer was formulated with low content. However, the nature of the amorphous drug obtained by spray drying had not been well investigated (Matsuda et al., 1992).

DSC analysis could be used as a quick screening tool for preformulation studies to study the potential incompatibilities of ingredients in the solid state (Fassihi, 1985). For the spray dried products, diclofenac sodium with different polymers did not show any characteristic transitions. None of the products showed any major addition or new peaks. The minor peak variations were perhaps due to difference in the moisture contents of the products as reported by Venkataran, Khohlokwane and Wallis (1995). From thermograms of the products, every formulations showed diclofenac sodium peaks, indicating that diclofenac sodium was present in solid state. The DSC results thus confirmed the existence of diclofenac sodium in solid form in the products.

From IR spectra and the thermal property results, spray dried amorphous form of diclofenac sodium exhibited the same chemical structure as that of the crystalline form. There was no interaction between the functional groups of the drug and the polymer, therefore the molecules were packed in the solid in a noncrystalline state (Matsuda et al., 1992). The diffraction pattern and the thermal property of diclofenac sodium in the microparticles suggested that some drugs were dispersed uniformly in the molecular level like a solid

dispersion in the polymer shell of the microparticles (Kawashima et al., 1992). In addition, it was found that the type of polymer and the polymer to drug ratio were the main factors affecting the crystallinity of the diclofenac sodium with polymer spray dried products.

Characteristic of the Spray Dried Products

For this study, a suspension feed was used. On drying a droplet atomized from a suspension feed, there was formation of a polymeric solid crust. Subsequently, the polymer formed an envelope around the drug crystal when atomized. The dried product was a microencapsulated drug crystal with a fairly smooth surface. Spray coating was preferable for the drug of low solubility in the feed medium where a suspension feed was used (Wan et al., 1990).

The spray dried particles were generally not of the matrix type. They were usually hollow spheres (Wan et al., 1991). This microparticle has been termed "microballoon" due its characteristic internal hollow structure. Diclofenac sodium was loaded in the outer shell of the microballoon (Kawashima et al., 1992). Based on the difference in drug crystallinity the resultant spray dried particles could be classified into two types: solid dispersed particles containing the amorphous drug and microcapsules of the drug with the polymer (Takeuchi et al., 1989). Preliminary X-ray diffraction and DSC measurements has shown that the drug present was in crystalline form and amorphous form in the solid state. Therefore, the drug could not be in a solid dispersion with the polymer. The matrix-like structure was constructed inside of the microcapsule (Kawashima et al., 1989). The drug release rate highly depended on those properties as will be discussed later.

Scanning electron microscopy was performed on the microballoons containing HPMC and ethylcellulose in the formulations (Formulations 1-7 and 11-21). The surface topography and the internal structure of the microballoons were investigated. The surface of the spray dried powder seemed to be entirely covered with polymeric materials. The spherical particles with a smooth surface and some surface shrinkages and folds were observed. The shrinkage of the surface wall was due to the entrapped air bubbles expanding considerably at higher drying temperature, a process that was offset partially by the loss of water. Deep indentations in the microballoons were also found occasionally, which was probably the result of water loss from the drying drop during the early stage of processing (Lin and Kao, 1991). The characteristic internal structure of the microballoon, a spherical cavity was enclosed with the rigid shell constructed with drug and polymer (Kawashima et al., 1992).

The formulation of microballoon prepared with the ratio of HPMC to diclofenac sodium at 1:2 (Formulation 1), revealed completely formed microcapsules with spherical shape and smooth surfaces; no crystals of drug were evident. At a lower inlet temperature, the drying of the droplet occurred slowly. Some evaporation of the solvent took place before the formation of the solid phase crust, resulting in shrinkage of the particles on drying. On the other hand, with a high inlet temperature, the solid phase crust formed quickly. The particles thus formed did not shrink as much (Wan et al., 1991). Microscopic analysis revealed that many diclofenac sodium crystals were present on the surface of the spray dried particles with ethylcellulose (Formulations 4-7). Takeuchi et al. (1989) observed that when the drug content was much higher than the polymer used, the drug crystallized without amorphism. They attributed this to the fact that undissolved drug in the feed would not undergo amorphism. High polymer content formulation gave rise to spherical particles with amorphous drug particles. Wan et al. (1990) had also

recommended that if the drug concentration far exceeded the polymer concentration, there would naturally be insufficient polymer to completely coat all the drug crystals. These uncoated crystals retained their crystalline structure. This finding explained the fact that the crystallinity of the diclofenac sodium with ethylcellulose microballoon was higher than those of the other formulations of microballoon.

On the surface of the microballoon containing low polymer content (< 30%), a number of pores were produced; the total pore volume of which depended on the type of polymer used and its concentration. As the concentration of the drug far exceeded the concentration of polymer, there would naturally be insufficient polymer to completely produce the microcapsules. Because of the initial drying of a droplet the moisture content fall to a critical value with the formation of a solid crust at the droplet surface. As the inlet air temperature was above the boiling point of the droplet solution, vapor was formed within the droplet, setting up pressure internally. Depending on the crust formed, the droplet may be punctured or "balloon". Such particles could not withstand mechanical handling and fragmented easily (Wan et al., 1990).

In the case of Formulations 8-10, the microparticles prepared with diclofenac sodium and chitosan generally had a porous and irregular sponge-like structure. The products were not hollow spheres. Apparently, there was no significant difference in their topographies, although chitosan was used in different amounts. While the combined formulations of diclofenac sodium with HPMC and chitosan spray dried products were of microparticles became sphere. On the contrary when the proportion of chitosan was increased, the shape of those became irregular. Wan et al. (1991) suggested that ineffective atomization at higher spray rates led to the formation of

irregular particles which were not completely dried when leaving the drying chamber. This resulted in the deposition of these irregular particles on the wall of the cyclone separator. Deposition on the drying chamber and cyclone collector was caused by very coarse droplets being formed in the spray and incomplete atomization (Masters, 1979).

In summary, it was found that the shape of the spray dried particles depended on the type of polymer and the spray rate of fed fluid for the spray drying condition. In addition, the shape of the spray dried particles also depended on the polymer to drug ratio in the formulation. When the content of the polymer in the formulation was high, the spray dried particles were spherical (Takeuchi et al., 1989). Conte et al. (1994) suggested that the polymer concentration in the solution to be sprayed might play an important role in microparticle formation; hence it would mainly affect the shape of microparticles. The surface became smooth when the inlet air temperature (Wan et al., 1990) and the concentration of polymer (Kawashima et al., 1989) increased. Kawashima et al. (1992) also stated that the complete microballoon without pores on the surface did not depend on the type of drug it contained.

Effect of the Operational Conditions in the Spray Drying Process

The solid particles could be directly formed by spray drying the droplets. Since this technique combines the drying and agglomeration process into one step, it might use least process time under good process control (Lin and Kao, 1989). The spray drying technique could be a very useful method for coating drug materials. The simplicity of the process and the possible use of aqueous solvents without the need for an additional drying step give it an added advantage over other microencapsulation techniques (Wan et al., 1991). The product properties might be governed by the polymer to drug ratio of solution,

inlet air temperature, feed spray rate and atomizing air pressure. The findings in this study showed that operational and formulation variations could have a marked effect on the properties of the microcapsules prepared by spray drying.

With the Niro apparatus, the outlet temperature could not be controlled directly, but it could be predicted with considerable accuracy from a knowledge of the inlet air temperature and the feed rate of solution, where in this study a range of 70-95° C was used. In order to avoid damage on the plant it must be controlled that the outlet temperature does not exceed 120° C; for many products 85-95° C will be suitable (Mobile Minor, Niro Spray Dryer Handbook). The outlet temperature of the dryer was determined solely by the main effects of the inlet temperature and the feed rate of solution. At a given inlet temperature, a decrease in feed rate will cause the outlet temperature to rise. The outlet temperature of the spray dryer was considered to be the most important factor in determining the residual activity of spray dried heat sensitive materials (Labrude et al., 1989). Similarly, it enabled the processing conditions to be controlled so as to give a desired outlet temperature. The extent to which this relationship would change with different formulations was uncertain, but it was unlikely to be substantially altered as long as the viscosity of the solution remained low (Broadhead et al., 1993). It has been reported that the moisture content of the product was determined by the outlet temperature of the spray dryer (Masters, 1979).

The moisture content of the final formulation was typically between 2 and 5% (Broadhead et al., 1994). This study clearly demonstrated the effect of ambient relative humidity on the moisture content of the product, and it would be desirable to carry out the spray drying process in a low humidity environment. Under these conditions, moisture levels of around 2 and 3% could be achieved. The effect of 75% relative humidity on the product moisture

content was observed in open containers at 45° C for 30 days. The moisture contents from the spray dried products runs carried out when the relative humidity was high were unacceptably high. It was believed that the powder weight increase depended on water permeability of polymer films. It could be concluded that Aquacoat (R) and chitosan films had better moisture protective property than did HPMC film when those films were sprayed with the formulations and with the conditions employed in this study.

In this study, spray drying allowed processing of even small batches to achieve good yields of production. The similar finding was reported by Conte et al. (1994). Nevertheless low yields were a persistent problem with laboratory-scale spray dryers (Broadhead et al., 1993). The spray dried products containing HPMC in the formulations significantly affect the reduction of the yield from the dryer. These formulations tended to adhere to the chamber wall, and lower yields were observed.

It was found that the percentage drug content was not affected by the processing variables used. The good uniformity of drug distribution in spray dried powder prepared from different conditions was obtained. These findings were attributed to the fact that the feed rate of solution offered excellent homogeneity of the drug and the polymer in solution. In addition, the drug contents varied with the shape of the spray dried particles. The drug content in the irregular particles of the spray dried products with chitosan was higher than the theoretical value. The drug content in the microparticles usually agreed well with the theoretical value expected from the formulation (Kawashima et al., 1988).

The spray dried products provided low bulk density. These findings might indicate that the particles from these products formed hollow structure. The

products from formulations that contained Aquacoat(R) and chitosan in the solutions exhibited higher bulk density than those of the other formulations. As a general rule, producing greater amounts of fine particles often formed a product of higher bulk densities because the greater number of smaller particles filled the voids between the larger ones, and the smaller particles might as well be more dense (Lantz and Schwartz, 1990). Results of measurement of bulk density and true density suggested that all the spray dried products were likely to have poor flow characteristics, as could be seen from the low value of bulk density and true density. The hollow microstructure and the extremely small particles of the spray dried products might result in higher porosity and lower bulk and true density, leading to the poor flow property of the spray dried powders. The flow properties, represented in terms of angle of repose of the microparticles, should be greatly improved if the particles were in matrix-like structures. These findings might be because the spray dried powders with chitosan in the formulations could form more irregularly-shaped particle which would lead to a reduction in the ability to flow. Compared to the sharp angular crystals present in the spray dried powders with ethylcellulose, these particles had better flow properties (Wan et al., 1990).

1. Effect of the Polymer to Drug Ratio

The effect of the polymer to drug ratio and the polymer concentration were the same as the results obtained by the aforementioned characteristics of the spray dried products. Kawashima et al. (1989) indicated that the main factors determining the size of microparticles were the concentrations of the drug and the polymer in the formulation. The average diameter of microparticles gradually increased with the weight ratio of polymer to drug in the system because of the increase in the number of aggregates of the microparticles.

2. Effect of the Inlet Air Temperature

In this study, three temperatures 130, 150 and 170 °C were used. The effect of the inlet air temperature was the same as the results obtained by the aforementioned characteristics of the spray dried products. The product moisture content was affected to a significant extent only by the drying temperature. An increase in drying temperature caused a reduction in the moisture content (Labrude et al., 1989; Broadhead et al., 1994). A tendency for the particle size to increase with increasing inlet drying temperature was observed. The similar finding was reported by Newton (1966). This effect was probably due, at least in part, to the increased tendency to agglomerate exhibited by the spray dried powders at high temperatures. In addition, the particle size of the product was greater than that obtained from a lower inlet temperature. "Ballooning" of the particles may also contribute to the increased particle size (Wan et al., 1990). The effect of temperature on particle size was reported to be dependent on the material being dried (Crosby and Marshall, 1958), and so this observation was probably formulation specific.

3. Effect of the Spray Rate of Feed

The spray dried products were prepared using different spray rates of feed, i.e. 14, 20 and 26 ml/min. The effects of the feed rate were the same as the results obtained by the aforementioned characteristic of the spray dried products. Theoretically, product size increases with higher feed rates. In this study, the spray dried particles were larger as the feed rate was increased. This result was in agreement with other investigators (Masters, 1979; Crosby and Marshall, 1958).

In addition, the diameters and distributions of the microparticle depended on the type of polymer used and its concentration (Kawashima et al., 1989). Higher percentages of fine powders were attained for the formulations with Aquacoat(R) and with chitosan. Wan et al. (1991) suggested that there was a limit to which the size of the particles could be increased without compromising the formation of well-coated products. To produce large well-formed microcapsules, increasing the feed rate is not recommended unless effective and complete atomization can be ensured. Masters (1979) described the products obtained from spray drying at various feed rates. At low feed rates, the droplet sizes were of high homogeneity. At higher feed rates, the atomizing air pressure could not penetrate the thick liquid jets. Atomization was incomplete and a wide droplet size distribution in the spray resulted. At high feed rates, therefore, it was important that the liquid feed had to first form into thin sheets to assist liquid instability for effective air to liquid contact and breakdown of liquid into ligaments or individual droplets. Unless "feed prefilming" took place, ineffective atomization resulted, even at high air velocities. Ineffective atomization at higher spray rates led to the formation of large particles which were not completely dried when leaving the drying chamber. This resulted in the deposition of these large particles on the wall of the cyclone separator (Wan et al., 1991). Therefore, only the fine particles left the chamber.

Seagar (1977) recommended that increasing feed spray rates would lead to a reduction in the outlet temperature and an increase in equilibrium solvent content or moisture level. Although the outlet temperature was decreased, the moisture levels of the spray dried products did not increase when higher feed rates were used. However, spray rates which were too low had the disadvantages of low efficiency with longer operation time and a high outlet temperature which may affect the exhaust tubings (Wan et al., 1991).

4. Effect of the Atomizing Air Pressure

The air pressure evaluated were 2, 3 and 4 bars in this study. The air velocity controlled the atomizing pressure required to breakdown the liquid feed into droplets. Atomizing pressure changes affected only the product size (Wan et al., 1991). Photomicrographs by scanning electron microscopy provided a better understanding of particle size and shape. Increased atomization pressure gave smaller particle size. This agreed with Masters (1979) that an increase in the energy available for atomization, in this case the rotary atomizer speed, was increased by air pressure and would reduce particle size.

Drug Release Behaviors of Microcapsules

The solubility of diclofenac sodium (pKa = 4.0) is markedly dependent on pH. Its rate of solution from microcapsules will therefore depend on the pH of the medium. As a microcapsule passes from the stomach into the intestine, it encounters a change in pH from about 1 to 7. Consequently, the residence time of the microcapsule in a particular hydrogen ion environment affects the availability of the drug from the microcapsule. In order to simulate the in vivo environment, experiments were run using a pH-changing medium. If a diclofenac sodium capsule is designed as a sustained release dosage form, it must conform to the USP XXIII specification : the continuous operation on the apparatus at stirring rate of 100 rpm.

The release rate of the spray dried powder was relatively slow in acidic pH media within the initial 2 hours. After potassium dihydrogen phosphate and sodium hydroxide were added, the medium pH changed from acidic to 6.8 and the release rate of drug increased rapidly (Lin and Kao, 1991). The release

of diclofenac sodium from the controlled release formulation tested is strongly medium dependent : faster dissolution is obtained in media without acidic stage or with higher pH values (Wilder, Detaevernier and Michotte, 1991). Examination of dissolution profiles of the drug diclofenac sodium with differing polymer quantities shows that as the polymer fraction increases, the dissolution of the drug decreased. The results of the dissolution study also indicated that the release rate in pH 6.8 medium could vary with the amount of the polymer added depending also on polymer type. This suggests that the releasing amount of diclofenac sodium also depends on the levels of the polymer used in the spray drying formulations.

The pH changed dissolution profiles of the spray dried diclofenac sodium with chitosan and of the spray dried diclofenac sodium with HPMC and chitosan showed no capability to control the drug release. Approximately 50-80% of diclofenac sodium were released in 3 hours from the irregular particles. This time period of release is unsuitable for a controlled prolonged release product. This complete ineffectiveness in controlling drug release was probably due to the shape of the spray dried particles, as the particle was a porous sponge-like structure. At this stage it was thought that incomplete microcapsule formation could be responsible for the rapid drug release from the particles. Apparently, the microparticle in this study had a matrix-like structure, which could slowly release the drugs without the burst sometimes found on the occasion of rupture of the reservoir (Kawashima et al., 1989).

1. Effect of Hydroxypropylmethylcellulose

Hydroxypropylmethylcellulose is cellulose ethers which may be used as the base for hydrophilic matrices for controlled release oral delivery (Hogan, 1989). Being independent of weight ratio, the release amount of diclofenac sodium from the microcapsules in pH 6.8 phosphate solution still depended on the amount of HPMC used. The reasons, as already explained, were attributed to the crystalline drug and complete coating. However, at a higher concentration of polymer, the polymer being hydrophilic, greatly improves the wettability of the drug and thus accelerates the dissolution (Wan et al., 1990). A successful hydrophilic matrix system requires polymeric substances that will wet and hydrate rapidly to form a gelatinous barrier. The rate of release is likely to depend on permeation through the barrier for water soluble drugs, and on erosion of the matrix for water insoluble drugs (Sheu et al., 1992). The release rate of diclofenac sodium spray dried with HPMC by pH changing system was fitted to the first-order release kinetic.

2. Effect of Ethylcellulose

The release patterns of diclofenac sodium from formulations containing the same amount of drug but different amounts of ethylcellulose showed that,as expected, the drug was released from matrices more slowly with an increase in ethylcellulose content; therefore, the release rate of drug could be modified by changing the ethylcellulose content in the matrices. When these matrices were brought in contact with water, a series of mass transport phenomena occurred. First, the pores near the surface of the matrix were filled by water and initial drug diffusion was controlled by the dissolution of the solute in the water-filled pores and by its continuous diffusion in water (Patomechaiviwat, 1993). As the amount of ethylcellulose increased, the release rate decreased and that was

found to be true for all formulations. This was attributed to the increase in the coat thickness and the path over which the drug diffused, and consequently the dissolution rate was reduced. The drug release profiles from the spray dried product with ethylcellulose would probably follow the first-order model.

3. Microcapsules of 1:2 Diclofenac Sodium to Single Polymer

Since diclofenac sodium dissolves poorly in acid medium therefore very low percentages of drug dissolved were observed in the first 2 hours. All the formulations of microcapsule showed slower dissolution than diclofenac sodium powder. Among these systems the dissolution of diclofenac sodium from ethylcellulose microparticle system was the slowest followed by those of diclofenac sodium from HPMC. Higher amount was to employ in order to yield slower dissolution since the dissolution retarding effect of any swellable polymer on a drug depends on the viscosity of polymer. Increasing the amount of the polymer in a matrix formulation increases the viscosity of gel layer and thus slows down drug diffusion (Alderman, 1984). However, increasing the amounts of HPMC in diclofenac sodium controlled release formulation would result in too much dose. This has also been reported by Dangprasirt and Ritthidej (1995).

In contrast, when ethylcellulose was used, the dissolution was so slow that only 63% drug dissolved after 24 hours. Ethylcellulose seemed to be a more suitable carrier since it gave continuous drug release up to 24 hours period. However, the initial stage of this dissolution profile was still too rapid. The burst in release of diclofenac sodium from microcapsules at the initial stage may result from the dissolution of drug crystals on the surface of microcapsules (Wan et al., 1991). Since the dissolution retarding effect on HPMC was obviously demonstrated, ethylcellulose, an insoluble polymer, and

HPMC, a swellable polymer, were used as combined carrier in an effort to improve the dissolution profile of diclofenac sodium microcapsules.

4. Effect of Polymer Combination Ratio

The mixture of polymers can have properties significantly better than an individual polymer for achieving controlled release (Akbuga, 1991). This paper concerns the use of cellulose polymers (HPMC and ethylcellulose) mixtures to control the release characteristics of diclofenac sodium microcapsules. Controlled release diclofenac sodium microcapsules were prepared with various combinations of HPMC and ethylcellulose, and release of drug from microcapsules containing these polymers in different ratios was studied. A wide range of release rates of drug can be obtained by a simple change in the ratio of polymers. Increasing the percentage of hydrophilic additives increases the release rate of drug from the microcapsules. This effect has been found by several authors who studied the effect of hydrophilic additives on spherical diffusion controlled systems (Gilligan and Po. 1991). These data showed that the results were in agreement with the first-order matrix model.

With increasing ethylcellulose concentration, the release rate of diclofenac sodium from microcapsules decreased drastically. The drug release rate could be controlled by ethylcellulose concentration. This may be due to polymeric properties of ethylcellulose. It is a hydrophobic polymer and insoluble in water. The dissolution profile of the microcapsules with HPMC and ethylcellulose at the polymers to drug ratio of (1:2):12 was so slow that only 78% drug dissolved after 24 hours. Since the ideal dissolution rate for the sustained release drug should follow the zero-order kinetics, a criteria was

set to look at the correlation coefficient of linear relationship between drug release and time.

As a conclusion, the combination of HPMC (hydrophilic polymer) and ethylcellulose (hydrophobic polymer) as a matrix in diclofenac sodium microcapsules was demonstrated to have a good potential in controlled release effect. The data revealed that by increasing the amount of HPMC or ethylcellulose in the matrix, an evident decrease in the drug release from microcapsules was obtained. It was found that the ratio of HPMC to ethylcellulose had a major influence on drug release rate. The similar finding had been previously reported by Gilligan and Po (1991).

5. Dissolution Pattern Compared to Commercial Product

In order to investigate the dissolution behavior of the commercial controlled release tablets, a controlled release diclofenac sodium products, Voltaren SR was studied. It had relatively uniform release pattern over a 24 hours period. The product was carried out with the pH changed dissolution method. The release of drug into a system which simulated the pH changes occurring in vivo during the passage of the drug from stomach to intestine showed a significant delay initially, during which time no drug appeared in solution. The lag phase persisted well after the acid condition had been neutralized. Voltaren SR tablet, a hydrophobic matrix tablet containing cetyl alcohol which is relatively hydrophobic, gave results similar to the low viscosity HPMC formulation. This may be due to the type of medium used which may cause precipitation of the drug at the surface of the tablet at an initially low pH (Sheu et al., 1992). When the medium pH was changed to pH 6.8, the tablet disintegrated and released its inner drug content, followed by a slower release until 24 hours. Thus, the commercial product possessed

sustained release function. Drug release from Voltaren SR was essentially a first-order process.

The amounts of drug release in 24 hours of spray dried products with ethylcellulose at the polymer to drug ratio of 1:2 and with HPMC and ethylcellulose at the ratio of (1:1):12, were closed to those of Voltaren SR. The release rate of spray dried products with ethylcellulose was relatively faster at the initial stage. This might be due to the fact that the spray dried products consisted of microcapsules which the surface was covered with microcrystals and could dissolve rapidly.

Conclusions

The findings showed that operational and formulation variations could have a marked effect on the properties of the microcapsules prepared by spray drying. The spray dried particles are simple matrix microcapsules, that is, a drug dispersion in the polymers. The four process variables, the polymer to drug ratio, the inlet air temperature, feed rate, and the atomizing air pressure in spray drying technique affected particle characteristics, particle size, moisture content, flowability, and density of powder. But these variables did not affect drug distribution in spray drying product. The percentage recovery of this technique was approximately 80%. Variations in the polymer to drug ratios not only affected surface properties but also the amorphism of the drug particles. In the case of HPMC, the polymer to drug ratio of 1:2 was desirable for the formulation of microencapsulated drug crystals with a complete microcapsule wall and the drug in the particle was in amorphous state. Knowledge of these effects can then facilitate the formulation of a product with the desired properties.

Diclofenac sodium controlled release matrix microcapsules could be prepared by spray drying method in aqueous conditions. The pH of dissolution medium affected drug release rate of all formulations in this study. Dissolution studies revealed that using only one polymer could achieve the effective controlled release system. The drug solubility and the polymer to drug ratio of solution were the main parameters to take into account in the realization of the optimal formulation. In selection of type and concentration of the polymer used in a combined formulation, the effect of concentration of both polymers on drug release pattern should be taken into account. The suitable polymers were HPMC at the concentration of 6.57% and the proper ethylcellulose latex dispersion at the amount of 13.14%. This product was cost effective and easy to prepare. This matrix microcapsules gave amount of drug release about 77.97% in 24 hours, the model of drug release would possibly be the zero-order model.