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The Improvement of Ibuprofen Dissolution Rate Through Microparticles Spray Drying Processed in an Aqueous System

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A study to enhance the dissolution rate of ibuprofen, a poorly water-soluble drug, was carried out through combining specific formulations and processes with the addition of a hydrophilic carrier for the preparation of microparticles. Microparticle production was performed by spray drying ibuprofen microsuspensions formulated in an aqueous system with the addition of ethanol containing Aerosil 200® and Tween 80®. We were able to consistently produce microparticles as much as 40% of the dry weight of the input microsuspension. Spray-dried microparticles were characterized by scanning electron microscopy, X-ray diffraction, differential scanning calorimetry, laser diffractometer mastersizer, and infrared spectroscopy. No modification to the crystalinity and chemical structure of ibuprofen was observed. Dissolution of ibuprofen microparticles reached 100% in 3 minutes compared with less than 10% for unmodified ibuprofen. We concluded that both by the modification of formulation and the spray drying process it is possible to increase the dissolution rate of the tested model drug.

Keywords ibuprofen; spray drying; microparticles; dissolution

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INTRODUCTION

Many of the current new active compounds are practically insoluble in water. Hence, the effort to increase their dissolution rate constitutes an essential step for the development of an oral solid dosage form. This, however, has proven to be a major challenge for formulators. As classified in the biopharmaceutics classification system (Amidon, Linnernäs, Shah, & Crison, 1995), the class II drugs (those with low solubility and high permeability) and class IV drugs (those with low solubility and low permeability) are characterized by irregular dissolution rates and, consequently, low bioavailability.

Several methods have been described to increase dissolution rates, such as chemical and physical approaches. Recently, formulators have devoted their time and efforts to develop solid dispersion systems (Leuner & Dressman, 2000) using hydrophilic excipients such as polyethylene glycol, polyvinylpyrrolidone, polyvinylalcohol, cellulose derivatives, polyacrylate, and polymethacrylates associated with surface active agents. Solid dispersions can be prepared in two ways: the hot melt method, whereby both the active substances and excipients are melted together, and the solubilization of drug and excipient in organic solvent, whereby both active compounds and carriers are sufficiently soluble, followed by the removal of solvent. The use of solid dispersion for commercial practice is limited by the problem of formulation, manufacturing and stability (Serajuddin, 1999; Chauhan, Shimpi, & Paradkar, 2005).

One of the factors that affect dissolution rates is the size of particles (Noyes & Whitney, 1897). Reducing particle size by micronization represents a technological possibility for enhancing the dissolution rates of pharmaceutical drugs. It is commonly used for the milling of raw materials and widely practiced in industries due to its advantages, such as low production cost and fast and easy scale-up. However, this process does have drawbacks, such as the electrostatic effects and broad particle size distribution. Additionally, it can also induce product disorder, whereby the disorder degree of the ground product is higher than that of the spray-dried product (Yonemochi et al., 1999).

Spray drying is an important application in the manufacturing of raw materials. It is also becoming important for the production of microparticles of dried active solutions and/or microsuspensions (Ermis & Yuksel, 1999; Fernandes, Vieira, & Veiga 2002). Spray drying is often used in the preparation of solid dispersion microparticles, whereby fine, dry powder particles can be produced at the same time. In contrast, the preparation of solid dispersion from solution using the evaporation technique causes the bulk of solid dispersion to be pulverized (Kim et al., 2006; Sethia & Squillante, 2004).

The use of organic solvents to obtain the complete solution of the active compound and excipient produces a residual hazardous waste. Other disadvantages include fire risks, environmental risks, and associated cost for industrial applications. The most feasible method to avoid the use of organic solvent is to shift to aqueous systems that are considerably safer pharmacologically, environmentally, and economically cheap and risk-free.

Ibuprofen is one of the propionic acid derivates widely used in the treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, and acute gouty arthritis; they also are used as analgesics for acute tendinitis and bursitis and for primary dysmenorrhea (Brunton, Lazo, & Parker, 2006). Its pKa is between 4.5 and 4.6 and it's practically insoluble in water (81 μg/ml) or acid medium but easily soluble in basic medium. The administration of a dosage of a conventional form of ibuprofen is inefficient biopharmaceuticallly and pharmacologically most of time due to its low dissolution. This can be minimized and overcome by increasing its dissolution rate. In this work, ibuprofen was then considered as a model drug.

Recently, various excipients and preparation methods have been used to increase the dissolution rate of ibuprofen. A β-cyclodextrin and its derivatives (methyl, hydroxyethyl, and hydroxypropyl β-cyclodextrin) are usually employed in the drug-excipient formation complex. These complexes were made by freeze drying an equimolar of β-cyclodextrin and its derivatives with ibuprofen in an aqueous ammonia solution (Mura et al., 1998). It was also prepared by passing a solution of ibuprofen in supercritical CO_2 through a methyl-β-cyclodextrin–packed bed (Charoenchaitrakool, Dehghani, & Foster, 2002). Hussein and colleagues (2007) used a controlled particle deposition method (CPD) whereby ibuprofen dissolved in supercritical CO_2 will permeate into the pores of the insoluble carrier (hydroxypropyl-β-cyclodextrin) and precipitate within. Another way to increase dissolution rate is by preparing its solid dispersion form. Here, ibuprofen was loaded onto microcrystalline cellulose (MCC) and cross-linked with polyvinylpyrrolidone (PVP-CL) by hot mix or solvent disposition methods (Williams, Timmins, Lu, & Forbes, 2005).

Another way to produce ibuprofen microparticles is by in situ micronization. The process was carried out with the method of instantaneous solvent exchange in the presence of stabilizing agents (i.e., hydrocolloids), which was then followed by spray drying (Rasenack & Muller, 2002a). Ibuprofen microparticles were also prepared by the addition of water as antisolvent into solvent coupled by lowering temperature gradually in the presence of surfactant with or without a polyethylene glycol (PEG) chain and hydrophilic additives as stabilizing agent (Rasenack & Muller, 2002b).

Polyethylene sorbitan fatty acid esters (Tween 80®) is a series of partial fatty acid esters of sorbitol and its anhydrides copolymerized with ethylene oxide (Rowe, Sheskey, & Owen, 2006). They are classified as hydrophilic nonionic surfactants and have been employed as additives for several purposes, such as to change the crystal properties of ibuprofen during recrystallization (Rasenack & Muller, 2002a), to stabilize the particles formed during the preparation of nanosuspensions and to increase dissolution rates (Kocbek, Baumgartner, & Kristl, 2006). Specifically, Tween 80®, a wetting agent, was used to stabilize microparticles with high surface energy that otherwise tend to agglomerate during suspension preparation (Merisko-Liversidge, Liversidge, & Cooper, 2003).

Colloidal silicon dioxide (Aerosil 200®) is submicroscopic fumed silica (Rowe et al., 2006). It was generally used as excipient in spray drying formulations to reduce the strong adhesion of the product to the spray drier wall as well as to increase the product yield (Billon, Bataille, Delalonde, & Jacob, 2002; Chauhan et al., 2005; Muller et al., 2000; Pohlmann, Weis, Mertin, Pesce da Silvera, & Guteres, 2000). Moreover, the dissolution rate of an active compound from solid dispersion prepared by spray drying containing Aerosil 200® was reported to be faster than spray-dried powder without Aerosil 200® (Friedrich, Fussnegger, Kolter, & Bodmeier, 2006; Takeuchi, Nagira, Yamamoto, & Kawashima, 2004).

In our earlier study (Wikarsa, Durand, Delalonde, Baylac, & Bataille, 2006), ibuprofen microparticles were prepared by the grinding of ibuprofen mixture, evaporation, and spray drying of the solution to find a suitable method of microparticle production. In the current study, we focused the use of a hydroalcoholic suspension of ibuprofen for microparticles production. Combination of the modification to the formulation and spray drying process has lead to several folds increase in dissolution rate. We propose that this method shall be extended to the industrial setting, where security, cost, and environmental pollutions are of concerns.

MATERIALS AND METHODS

Materials

Ibuprofen, colloidal silicon dioxide (Aerosil 200®), and polyoxyethylene sorbitan monooleate (Tween 80®) were purchased from Global Bulk Drugs and Fine Chemicals Limited (Kohir Mandal, India), Degussa AG (Essen, Germany), and Cooper Melun (Melun, France), respectively. Sodium hydroxide, potassium dihydrogen phosphate, and ethanol were purchased from Fluka (Seelze, Germany).

Methods

Microparticle Preparation

Microparticles were produced from ibuprofen microsuspension comprising two phases, the alcoholic phase, where ibuprofen and Tween 80® were dissolved in alcohol, and the water phase, where Aerosil 200® was dispersed in water. The concentration of ibuprofen and alcohol used were fixed at 10 and 12% respectively. The concentrations of Tween 80® and Aerosil 200® used were varied 0.25%, 0.5%, and 1% for Tween 80®, and 0.0%, 0.5%, 0.75%, 1%, and 1.5% for Aerosil 200®. A 100 gram mixture containing the two phases was used for each experiment. Formulations are presented in Table 1. Once the two phases were mixed, they were immediately exposed to a high shear mixing at 9,300 rpm for 3 minutes, utilizing Ultra Turax Cell disrupter (type 18/10, Jake and Kunkel IKA-WERK, Staufen, Germany) to prevent the growth of resulting ibuprofen crystals. The microsuspension was then spray dried in a Mini Buchi 190 (Buchi Labortechnik AG, Flawil, Switzerland) under standardized conditions obtained during preliminary studies: inlet temperature 90 °C, outlet temperature 65 °C, air flow 600 Nl/h, aspirator stream 50m^3/hour, and suspension flow 5.4 g/minute using a 0.5-mm nozzle.

TABLE 1
Composition of 100 g Suspension to Spray Dried Aerosil 200® (A), Tween 80® (T), and Water (W)

Formulation	A (%)	T (%)	W (%)
1	1.50	0.25	76.25
2	1.50	0.50	76.00
3	1.50	1.00	75.50
4	1.00	0.25	76.75
5	1.00	0.50	76.50
6	1.00	1.00	76.00
7	0.75	0.25	77.00
8	0.75	0.50	76.75
9	0.75	1.00	76.25
10	0.50	0.25	77.25
11	0.50	0.50	77.00
12	0.50	1.00	76.50
13	0.00	0.25	77.75
14	0.00	0.50	77.50
15	0.00	1.00	77.00

Microparticle Physicochemical Properties

For each experiment, the yield was determined as the percentage of the dry weight of microparticles relative to the dry weight input/raw material. Microparticles produced from formulation 5 were selected for further quality control due to its high yield of atomization (42.12%) and in moderate excipient concentrations (1% Aerosil 200®, 0.5% Tween 80®; Table 2).

Morphology. The morphology of original ibuprofen and spray-dried ibuprofen microparticles were analyzed by scanning electron microscopy (Hitachi S 4000, Tokyo, Japan; SEM). Prior to scanning, samples were mounted on double adhesive tape and sputtered with a thin gold-palladium coat (Bal-Tec, CPD 030, Balzer, Switzerland).

Particle Size. The size of the original ibuprofen and the size of the microparticles produced were determined using a Laser Diffractometer Mastersizer X (Malvern Instruments Limited, Worcestershire, UK). Diameters for 10%, 50%, and 90% of particle size population were recorded.

X-ray Diffraction (XRD). Powder XRD patterns were obtained by automatic Philips Diffractometer X-ray. The samples were irradiated with monochromatized Cu K_α radiation (0.15405 nm) and analyzed between 2 and 20 °θ. The patterns were collected at a voltage of 20 kV and a current of 40 mA, respectively.

Differential Scanning Calorimetry (DSC). Differential scanning calorimetry studies were carried out using a DSC6 calorimeter (Perkin-Elmer Instruments, Beaconsfield, Bucks, UK).

TABLE 2
Ratios of Aerosil 200®/Tween 80® (I/T) and Spray Drying Yields

Aerosil 200® (%)	No Formulation	A/T Ratio	Yield (%) ± *SD*[a]
1.5%	1	6.00	39.67 ± 0.58
	2	3.00	41.57 ± 0.00
	3	1.50	42.96 ± 4.66
1.0%	4	4.00	38.73 ± 6.91
	5	2.00	42.12 ± 1.33
	6	1.00	25.82 ± 4.56
0.75%	7	3.00	35.60 ± 0.62
	8	1.50	31.58 ± 5.51
	9	0.75	19.16 ± 1.62
0.5%	10	2.00	39.75 ± 7.67
	11	1.00	26.57 ± 1.75
	12	0.50	4.61 ± 0.18
0.0%	13	0.00	0.00
	14	0.00	0.00
	15	0.00	0.00

[a]*SD*=standard deviation.

Indium/zinc standards were used to calibrate DSC temperature and enthalpy scale. The samples were hermetically sealed in aluminium pans and heated at a constant rate of 20 °C/minute. at a temperature from 20 °C to 100 °C under nitrogen purge at a flow rate of 30 ml/minute.

Infrared Spectroscopy (IR) Analysis. The infrared spectra of original ibuprofen, Tween 80®, Aerosil 200®, and spray-dried microparticles were analyzed by a Perkin-Elmer 983G spectrophotometer. A KBr pellet was initially formed by mixing 2% of a sample with dried KBr using a mortar and pestle, and afterward by compressing 100 mg of the mixture under a force of 10 tons in a punch-and-die set to form a transparent KBr pellet. The pellet was carefully transferred onto a sample holder. The samples were examined in transmission mode over wave number range of 4,000 to 185 cm^{-1}.

In Vitro Dissolution Studies. Dissolution profiles of the spray-dried microparticles were obtained from a paddle rotating dissolution apparatus (Direction de la Qualité du Medicament du Conseil de l'Europe, 2005) using an ERWEKA DT6R as a dissolution tester. Spray-dried powders (equivalent to 200 mg of ibuprofen) were introduced into 900 ml of dissolution media phosphate buffer at a pH of 6 maintained at 37 ± 1°C, with the rotating paddle set at 50 rpm. Samples were automatically collected at regular intervals using a peristaltic pump over a period of 30 hours and assayed spectrophotometrically at 223 nm (Perkin-Elmer λ 15, Waltham, USA).

Physical Stability. The stability of ibuprofen microparticles was tested by storing the hermetically closed sample at 25 ± 1° C. Periodically (1 and 6 months after preparation), samples were removed and characterized by DSC, XRPD studies, and dissolution rate measurements.

RESULTS AND DISCUSSION

Preliminary experiments were carried out to determine the influence of formulations (addition of excipients) and spray drying process on the dissolution rate of a model drug. To generate a good substrate for spray drying, 2 features were added: surfactant as a dispersing agent and wetting purpose and drying agent to increase yield.

In this study, the microsuspensions of ibuprofen containing Tween 80® with or without Aerosil 200® in an aqueous-alcoholic system were spray dried under the following predetermined conditions on the spray dryer: inlet temperature of 90°C; outlet temperature of 65 °C; air flow of 600 Nl/hour; aspirator stream of 50m^3/hour; and a suspension flow of 5.4 g/minute using a 0.5-mm nozzle. These production parameters were obtained from preliminary experiments, where nozzle size and air flow were fixed as constant parameters. The optimal values for inlet temperature, aspirator stream, and suspension flow were obtained, and the values that give the highest yield, lowest residual moisture content and highest ibuprofen content were used for all subsequent experiments. To investigate the optimum concentration of Aerosil 200® and Tween 80® for microparticle production, we tested several formulations, varying the ratios of concentration used, and evaluated the effects ratios have on microparticle yield. The results are presented in Table 2.

As presented here in Table 2, the results showed that at 1.5% Aerosil 200® (formulations 1–3), the yields of microparticles were not affected by the changes in Tween 80® concentration. At Aerosil 200® concentration lower than 1.5%, the increase in Tween 80® concentrations reduced the yields significantly (formulations 4–15). At 0% Aerosil 200®, no microparticles were produced, signifying its necessity for the procedure used in this study (formulations 13–15).

We can postulate that these results reflect on both the formulation and the process. With respect to the formulation point of view, the excipient and its proportion are essential. Tween 80® belongs to the chemical family of polyoxyethylene sorbitan fatty acid esters (Rowe et al., 2006) with a 149 flash point value. This waxy material cannot be easily dried in the spray dryer, as it will stick to the column and reduce yield.

Aerosil 200® is a colloidal silicon dioxide (Rowe et al., 2006) widely used in pharmaceutical formulations. In the spray drying process, this raw material is recognized for improving flowability and yields of production. When it was formulated with a waxy material, colloidal silicon dioxide was an excellent adsorbent and anti-adherent agent (Chauhan et al., 2005), favorable for the spray drying process (Pohlmann et al., 2000). In the formulations tested, we hypothesized that the ability of Aerosil 200® to adsorb portions of Tween 80® and ibuprofen contributed to the reduction of sticking and the increase in yield.

From the process aspect, with the lab-scale apparatus used here, most of the sprays resulted in low yields, because of powder deposition on the column and cyclone walls and difficulties in collecting spray-dried particles, especially the smaller ones (Prinn, Constantino, & Tracy, 2002; Maa, Nguyen, & Hsu, 1998). It was reported that with such standard apparatus, the powder trapped in the exhaust air filter account for approximately 15% to 20% of the total solid, consisting primarily of particles less than 2 μm, which was attributed to the failure of the cyclone to collect fine particles effectively. Alternatively, their low masses caused them to be drawn up into the exhaust (Maa et al., 1998; Prinn et al., 2002).

SEM and Particle Size

SEM images are presented in Figure 1. Original ibuprofen (1a) consisted of colorless crystals with a 50% population at 76.55 μm, as obtained by laser diffraction analysis. Spray dried formulated ibuprofen consisted of microparticles with significant size reductions with half of the particle population at 6.07 μm. As previously described (Rasenack & Muller, 2002a, 2002b) and observed in our experiments, this size reduction or in situ micronization was formed when the antisolvent (aqueous system) and solvent (alcoholic system) were mixed under

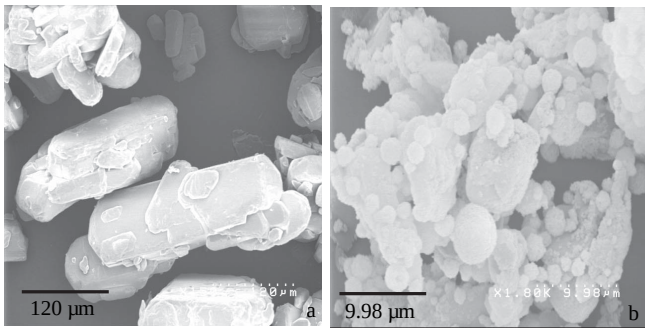

FIGURE 1. SEM image of (a) original ibuprofen and (b) ibuprofen microparticles (formulation 5).

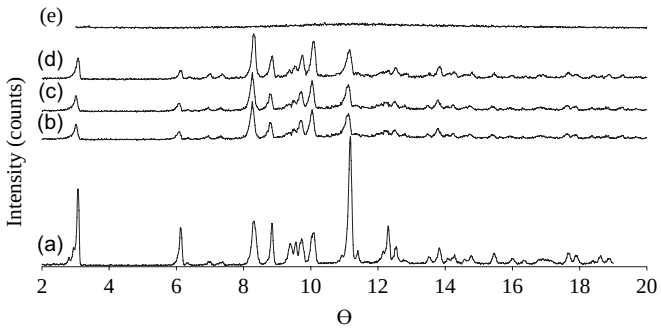

FIGURE 2. XRD of (a) original ibuprofen, (b) initial ibuprofen microparticles (formulation 5), (c) after 1 month, (d) 6 months, and (e) Aerosil 200® .

TABLE 3
Measured Particle Size of Original Ibuprofen and Spray Dried Ibuprofen Microparticles

Formulation	d (0.1) µm	d (0.5) µm	d (0.9) µm
Original ibuprofen	13.37	76.55	231.60
Ibuprofen microparticles (formulation 5)	2.59	6.07	14.67

high stirring conditions (Ultra Turax at a rotation speed of 9,300 rpm in present work) prior to spray drying. We hypothesized that the powder obtained could be a matrix of ibuprofen, Tween 80®, and Aerosil 200®, or ibuprofen microparticles coated by Tween 80® and Aerosil 200®.

XRD

XRD patterns of original test ibuprofen (Figure 2a) were characteristic of a crystalline structure, with specific diffraction peaks at θ=3.08 and 11.8. The pattern of microparticles after processing (Figure 2b) did not show significant differences in the d (interplanery distance) and spacing values with only slight decrease in peak intensity, which could be explained to be due to dilution effect (Kamble, Maheshwari, Paradkar, & Kadam, 2004). However, the relative intensities of certain XRD peaks did change. This was attributed to the markedly different crystal habits of the samples. Therefore, the relative abundance of the planes exposed to XRD sources would have been altered, producing the variation in the relative intensities of the peaks. Alternatively, this might be due to differences in the crystal sizes (Garekani, Sadeghi, Badiee, Mostafa, & Rajabi-Siahboomi, 2001). To further investigate the crystallinity state, a stability study was carried out. The XRD analysis was performed on ibuprofen microparticles after storage of 1 month (2c) and 6 months (2d). These results revealed that the spray-dried powders have had the same patterns. These results confirmed that crystalline ibuprofen composite had a high stability.

DSC

As presented in Figure 3, the onset melting point values of unmodified ibuprofen and spray-dried microparticles at 0, 1, and 6 months of storage were 74.7°C (ΔH = 120 J/g), 72.1°C (ΔH = 75 J/g), 72.2°C (ΔH = 77 J/g), and 72.4°C (ΔH = 78 J/g), respectively. The onset melting point value of spray-dried ibuprofen microparticles was slightly lower than that of the unmodified ibuprofen due to the presence of Tween 80® (waxy material; data not published), as has previously been described by Kamble and colleagues (2004). Since no exothermic peak was observed for the microparticles, we concluded that there were no changes in cristallinity.

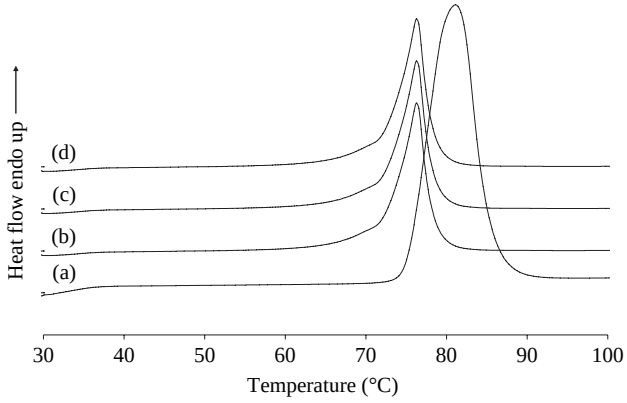

FIGURE 3. DSC thermograms of (a) original ibuprofen, (b) initial spray-dried ibuprofen microparticles (formulation 5), (c) after 1 month, and (d) 6 months.

IR Spectroscopy

In a single ibuprofen crystal cell, four ibuprofen molecules are connected by two hydrogen bonds (Romero, Savastano, & Rhodes, 1993). The two remaining carboxylic groups are available for binding to neighboring unit cells. Thus, in the crystal structure of ibuprofen, the hydrophilic structures are mutually bonded, producing a hydrophobic crystal structure.

Ibuprofen infrared spectrum (Figure 4a) showed a very broad band occurring between 3,300 and 2,000 cm^{-1}, which can be assigned to νOH stretching mode of hydrogen bonding associated dimmers. The broad strong band at about 1,722 cm^{-1} is attributed to νC=O asymmetric vibration of the COOH dimmer group. Similarly, the strong band at about 1,232 cm^{-1} is assigned to νC-O stretching. The strong bands corresponding to the OH associated group of ibuprofen as well as the broad bands, assigned to the stretching vibration of C=O and C-O groups, indicated the existence of associated dimmers by intermolecular hydrogen bonding.

Figure 4a, two bands observed at 3,094 and 3,020 cm^{-1} according to the compound, could be assigned to aromatic νCH, while three bands at 2,955, 2,921, and 2,869 cm^{-1} were attributed to aliphatic νCH_2 and νCH_3. Also, several bands occur between 1,506 cm^{-1} and 1,420 cm^{-1}, which were assigned to aromatic C=C and aliphatic δCH_2 and δCH_3 bending vibrations. However, the interaction between drug and excipients often leads to identifiable changes in IR profile.

In fact, comparisons made with spectra (4a-4c) of ibuprofen, Tween 80®, or Aerosil 200® revealed the spectrum of the spray-dried microparticles (Figure 4d) to be a simple overlay of the spectra of both components, confirmed by the stretching νC=O band around 1,722 cm^{-1} and the stretching νC-O band around 1,232 cm^{-1} appearing at the same wavelength.

In Vitro Dissolution Studies

Studies were carried out under sink conditions. A phosphate buffer of pH 6 was selected to distinguish the dissolution rate of the drug, allowing a greater discrimination of the effect of the process and thus of formulations. As presented in Figure 5, the dissolution profile of spray-dried ibuprofen microparticles (c) was approximately 10 times higher than the unmodified drug (a). Ibuprofen from microparticles was all released within 3 minutes.

There are various explanations for these results. First, as previously indicated by laser diffraction measurements and SEM microphotographs, spray-dried microparticles have a significantly smaller particle size. Consequently, the surface contacts between microparticles and dissolution medium increases, allowing quicker dissolution to release the active component.

Second, there is a plausible role of formulation. Tween 80®, a wetting dispersing/suspending excipient, is composed of a series of partial fatty acid esters of sorbitol (hydrophobic part) and its anhydrides copolymerized with ethylene oxide moles (hydrophilic part). This particular chemical structure contributed to the absence of particle growth, reducing agglomeration phenomena during the preparation and spray drying of the microsuspension. As a result, surface wettability increased for processed products, inducing faster dissolution rates.

Moreover, Aerosil 200® is a hydrophilic colloidal silicon dioxide that would contribute in the formation of hydrophilic matrix powder and increase wettability and dissolution rate. As demonstrated in the IR spectroscopy analysis, the chemical interaction didn't occur in spray-dried microparticles. The increase in dissolution rates was not caused by chemical interaction. Finally, and as summarized in Figure 5 (c and d), dissolution profiles obtained on samples tested after storage for 1 month and 6 months showed excellent stability without significant differences in terms of kinetics and drug release quantity.

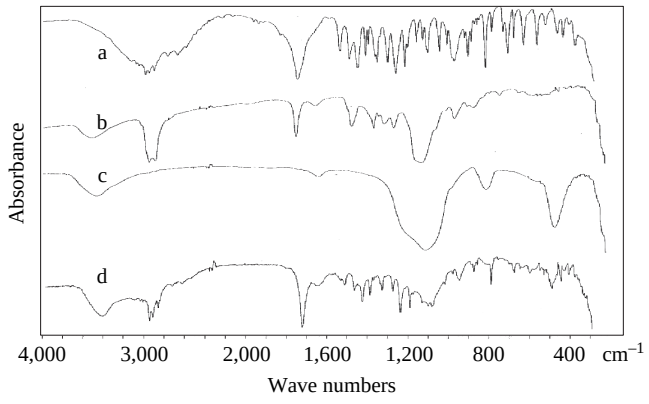

FIGURE 4. Infrared spectra of original ibuprofen (a), Tween 80® (b), Aerosil 200® (c), spray-dried ibuprofen microparticles (formulation 5) (d) in 4000-185 cm^{-1} region.

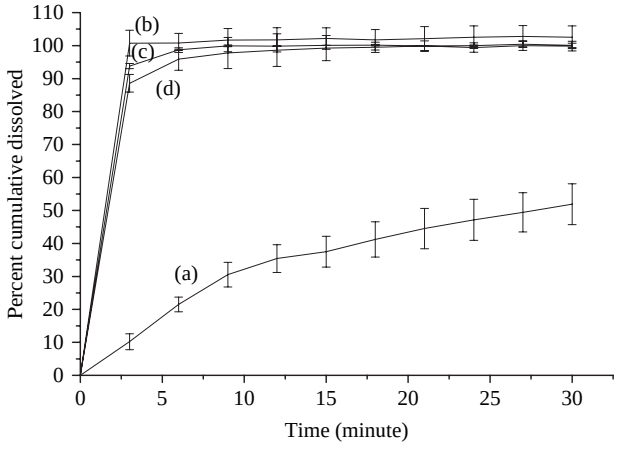

FIGURE 5. Dissolution profiles of ibuprofen from (a) original ibuprofen, (b) initial spray-dried ibuprofen microparticles (formulation 5), (c) after 1 month, and (d) 6 months.

CONCLUSION

The spray drying process was developed to prepare microparticles of a model drug recognized for its poor water solubility. The approach utilized a combination of distinct formulations and processes to improve the dissolution rate of such a drug in a hydroalcoholic system. In the experimental conditions, spray drying of ibuprofen in a water dominant medium was successful if a microsuspension contained surfactant and a common drying agent such as Aerosil 200®. In vitro dissolution studies showed that the spray-dried microparticle had a better dissolution profile. There was no modification to the chemistry and crystallinity of ibuprofen, which are stable for at least up to 6 months postproduction. The spray drying procedure utilized in our study should offer an interesting alternative for the development of active microparticles from a poorly water-soluble drug for the purpose of preparation of oral solid dosage forms.

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