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RESEARCH PAPER

Some Physicochemical Properties of Mefenamic Acid

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ABSTRACT

Mefenamic acid is a problematic drug in granulation, tableting, and dissolution due to its poor solubility, hydrophobicity, and tendency to stick to surfaces. In most cases, the specifications of a drug by the pharmacopoeia include identification and purity, but they do not describe the physicochemical drug properties precisely. To characterize the mefenamic acid particle size, surface area measurements, X-ray pattern, differential scanning calorimetry (DSC), wettability, crystal habit, and compression behavior of different batches from two manufacturers were investigated. Due to larger particle size and better wettability, mefenamic acid of Il Yang type was easier to handle in a granulation process. The compression behavior of both types was nearly the same, although particle size, crystal habit, and wettability were very different.

Key Words: *Differential scanning calorimetry; Force-time profiles; Mefenamic acid; Physicochemical properties; X-ray diffraction; Surface area.*

INTRODUCTION

Mefenamic acid is a high-dose nonsteroidal anti-inflammatory agent prepared as immediate-release capsule and tablet formulations. It is a poorly soluble drug in aqueous media (1), sticking to any type of surface, and is not easy to handle in granulation and tableting processes. As is the case for many poorly soluble drugs, dissolution of mefenamic acid is a problem. To facilitate tabletability, enhance dissolution rates, and develop a sta-

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ble and reproducible dosage form, it is necessary to investigate the physicochemical properties of mefenamic acid and batch-to-batch variation.

As often described in the literature, particle size distribution and surface area of the drug are important parameters that affect dissolution. Itai et al. (2) evaluated the influence of particle size and wetting agents on the dissolution rates of flufenamic acid in relation to surface area. According to the Noyes-Whitney equation, they calculated the solubility C_s of the drug in phosphate buffer, pH 6.24, and the dissolution constant k at various concentrations of Tween 80. The solubility and k did not change at concentrations below the critical micelle concentration (CMC), whereas above the CMC, the solubility was increased due to decreasing surface tension and the micellar solubilization of the drug. Reduction of the particle size led to considerable enhancement of the dissolution rates.

The preliminary step for dissolution, tablet disintegration, and also wet granulation is the wetting of the solid surface. Wetting can be described as the replacement of the air on the solid surface by a liquid (3). It can be investigated by direct measurements of the solid-liquid contact angle using the sessile drop method or the Wilhelmy plate method. For these measurements, the powder must be compressed into a tablet of exactly defined dimensions without using any excipients, which is feasible for many types of powders. Another problem arises from the penetration of the liquid into the tablet. As a result, the measured angle varies with time, and dissolution of the drug by the liquid may occur.

According to Washburn (4), the contact angle can be alternatively determined by indirect measurement of the liquid penetration rate into a powder bed. The Washburn equation describes the flow of liquids in a capillary. Since a powder bed has many capillaries with varying radii, the Washburn equation has to be modified to describe the flow in capillary bunches considering the porosity of the powder bed and assuming a constant radius $\bar{r}$. A material constant has to be determined by adsorption of a liquid in which the drug is completely insoluble, assuming a contact angle of zero. In most cases, the constant can be determined by adsorption of *n*-hexane. Because the determination of the height of the liquid in the powder bed is difficult, it can be replaced by determination of the weight increase. When the weight increase versus time is plotted, the slope of the curve before reaching the plateau provides information about the dimension of the wettability.

In this study, the wetting behavior of mefenamic acid was characterized by adsorption of various solutions containing different concentrations of sodium dodecyl sulfate (SDS) and Tween 80. To verify whether the differences in the wetting behavior measured by the Washburn method are important for drug release, in vitro dissolution rates of mefenamic acid bulk drug capsules were carried out in Tris buffer, pH 9, containing the same concentrations of surface-active agents. In the literature, various studies concerning the influence of surface-active agents on the release rates of drugs that are practically water insoluble are described. Crison et al. (5) investigated the effect of surfactant purity on the dissolution rates of the water-insoluble drug carbamazepine and found a higher wettability and dissolution rate for surfactants of higher purity. Ghanem et al. (6) studied the solubilization of flufenamic acid using different nonionic surface-active agents.

Other important parameters that influence dissolution are polymorphism and crystallinity of the drug. The dissolution behavior of different polymorphic forms of mefenamic acid was evaluated by Aguiar and Zelmer (7). They found that the metastable polymorph II has a higher saturation solubility than polymorph I, but in the dissolution media, polymorph II was unstable and was completely converted into polymorph I. The limiting step in the dissolution process was therefore attributed to the poor solubility of polymorph I. Clinical tests with 500 mg mefenamic acid bulk drug capsules, however, demonstrated that there was no significant difference in absorption due to the small free energy difference of the polymorphs. To characterize the polymorphism of various batches of mefenamic acid, diffferential scanning calorimetry (DSC) and X-ray patterns were investigated in this work.

The crystal habit of a drug can also affect the tableting process. Haleblian (8) described that one crystal habit of a drug may be easily compressible, while another may cause problems, with both showing the same melting point and X-ray pattern. Joiris et al. (9) determined the compression behavior of different types of paracetamol. The orthorhombic paracetamol exhibited better tabletability than the monoclinic form due to the presence of parallel sliding planes. Thus, some scanning electron microscopy (SEM) micrographs were taken to describe the crystal habit of the different mefenamic acid batches. To examine the compression behavior, force-time curves were registered and compared to the curves of Starch 1500, which is known to exhibit plastic deformation, as well as elastic components.

EXPERIMENTAL

Materials

Different batches of mefenamic acid Il Yang Metha (Pharm. Co., Ltd., Seoul, Korea) and Chimica Synthetica

(Barcelona, Spain) were examined. A portion of one Chimica batch, lot 1116036, was pretreated with gradient grade *n*-hexane (Merck KGaA, Darmstadt, Germany) before examination and was named lot 1116036H.

SDS (Henkel KGaA, Düsseldorf, Germany) and Tween 80 (Deutsche ICI GmbH, Essen, Germany) were EP quality.

For force-time profiles, Starch 1500 (Colorcon GmbH, Königstein, Germany) was used as the reference material.

Particle Size Distribution by Laser Diffraction

The particle size distribution was determined using a laser diffractometer (Sympatec Helos KA Compact, Sympatec GmbH, Clausthal-Zellerfeld, Germany) with a dry dispersing system RODOS at 100 mm focal length. The pressure was adjusted to 4 bar, and the injector suction was at maximum level. Before the measurements were started, the laser beam was focused onto the central segments of the detector to simulate measuring conditions without powder. The measurements were done in triplicate at an optical density of 3–6% and intervals of 10 sec. Evaluation of the spectra was done by Windox Software version 3.1 (Sympatec) on an IBM-compatible personal computer (HP Vectra VL, Hewlett Packard, Boeblingen, Germany).

Surface Area Measurements

The determination of surface area was performed using a Coulter SA 3100 (Coulter Electronics, Krefeld, Germany). Data evaluation was done according to Brunauer-Emmett-Teller (BET) theory (10). The samples were degassed in 9-ml sample tubes for 1 hr at 80°C in a vacuum. Free-space measurements were done using helium; surface area measurements were performed by adsorption of nitrogen (both from Messer Griesheim GmbH, Krefeld, Germany). Both gases were class 5.0 pure. The measurements were carried out using a 10-point BET mode at high sensitivity and a relative pressure range between 0.05 and 0.3 p/p_0. Each batch was measured three times, and the mean surface area was calculated.

Determination of Wettability

The wettability of mefenamic acid was determined using a Krüss processor tensiometer K12 (Krüss GmbH, Hamburg, Germany) by adsorption of solutions containing different concentrations of surface-active agents. For each measurement, 1.6 to 1.8 g of mefenamic acid, exactly weighed, were filled onto a filter paper (FP1212) in a Washburn cylinder (Fibre Chamber FL 12 for Krüss processor tensiometer K12) and compressed by the piston to a porosity of 0.44 to 0.50. The Washburn cylinder was placed on the balance of the tensiometer, and the measurement was started. The beaker containing liquid was lifted until a weight increase of 0.0005 g registered on the tensiometer connected to the IBM-compatible personal computer using K121 software, version 2.04.a (Krüss). The adsorption of the solution was determined at intervals of 0.5 sec until a plateau was reached.

The Washburn constant was determined for each batch of mefenamic acid by adsorption of *n*-hexane assuming a contact angle of zero. Aqueous solutions of SDS and Tween 80 were prepared for adsorption measurements in volumetric flasks filled with bidistilled water and equilibrated for 24 hr at room temperature before use. The adsorption of SDS was done for each batch of mefenamic acid, while the adsorption of Tween 80 was determined for only Il Yang lot 1069015 and Chimica lot 1116036. Each measurement was done in triplicate for each concentration of surface-active agent at 20°C. Concentrations ranging from 251.77 mg/L to 598.45 mg/L for SDS and 260 mg/L to 2004 mg/L for Tween 80 were used. The surface tensions of the solutions were measured at 20°C using the Krüss processor tensiometer K12 and the Wilhelmy plate technique with a roughened platinum plate.

Dissolution Rates

Dissolution rates of mefenamic acid bulk drug capsules were determined in 540 ml of dissolution medium using a paddle apparatus according to USP 23 at a paddle speed of 100 rpm and a temperature of 37°C. The medium consisted of Tris buffer (pH 9.0) and different concentrations of SDS and Tween 80. The capsules were filled with 300 mg of mefenamic acid Il Yang lot 1069015 or Chimica lot 1116036. The released drug was determined by ultraviolet (UV) spectroscopy at $\lambda = 332$ nm using a Perkin Elmer S550 spectrophotometer (Perkin Elmer, Stuttgart, Germany).

Differential Scanning Calorimetry

Polymorphism and melting points were examined using a Mettler DSC 820 (Mettler Toledo, Gießen, Germany). The drug, in exactly weighed 10-mg samples, was put in standard aluminum pans with perforated caps. The samples were heated from 25°C to 225°C at a heating rate of 20 K/min, cooled, and stored at room temperature

for 7 days before they were heated again from 25°C to 300°C at the same heating rate.

X-Ray Powder Diffraction

Powder diffraction patterns of all batches were determined using a PW3710 diffractometer (Philips, Eindhoven, Netherlands) with CuK_α radiation. The sample tubes were filled completely with mefenamic acid and measured at a generator tension of 40 kV and a generator current of 40 mA.

Scanning Electron Micrographs

The crystal habit of the drug was examined by SEM using a DSM 940 A (Carl Zeiss, Oberkochen, Germany). The samples were fixed on aluminum pins by Tempfix, a double-adhesive tape, and coated with gold using a sputter coater E5100 (Bio-Rad GmbH, Munich, Germany). The samples were sputtered four times for 60 sec and exposed to 20 mA current and 2.1 kV voltage. The micrographs were taken at 5 kV and a magnification of 200.

Force-Time Curves

The force-time curves of mefenamic acid lots 1069015 and 1116036 were determined according to Schmidt and Vogel (11) by putting 250 mg of mefenamic acid, exactly weighed, into the 10-mm die of a rotary tablet press (Pharmapress 230, Korsch Pressen, Berlin, Germany) by hand. Compression was done as single tablets without lubrication using 10-mm, flat-face, beveled-edge punches at compression force levels of 5 and 10 kN. Data were acquired and evaluated by TurboLab, version 4.2 (Stemmer Software GmbH, Puchheim, Germany). The compression curves were standardized to 5 and 10 kN by $F_{stand} = F^*(5 \text{ or } 10)/F_{max}$. After compression, the area quotient A6/A5 was determined and compared to compression parameters of Starch 1500, which was compressed as described above.

RESULTS AND DISCUSSION

Particle Size Distribution and Surface Area

The particle size distributions and data of the surface area measurements are shown in Table 1. Lot 1069015 had a mean particle size of 12 μm and a surface area of 0.92 m^2/g. The other Il Yang batches had larger particle sizes, about 18 μm, and hence a smaller surface area, about 0.7 m^2/g. As compared to Il Yang batches, Chimica batches exhibited lower mean particle sizes (9.17–10.8 μm) and relatively smaller surface areas (0.85–0.74 m^2/g). In both cases, however, the batch with the largest particle size showed the smallest surface area. Chimica lot 1116036 did not show any change in particle size distribution and surface area after *n*-hexane treatment, indicating that no drug dissolution took place.

Wettability of the Drug

Figure 1 shows the adsorption rate of SDS solutions onto mefenamic acid. The concentration of SDS, and hence the surface tension of the liquid, had no influence on the adsorption rate of Chimica mefenamic acid. The adsorbed amount was very low, and both batches showed the same wetting behavior. The adsorption rate of Il Yang batches increased with increasing SDS concentration. Lot 1069015 showed the lowest adsorption rate. The poor wettability of the Chimica batches and Il Yang lot 1069015 might be due to the increased hydrophobicity caused by smaller particle sizes (2).

Figure 2 shows the wettability of both mefenamic acid types by Tween 80 solutions. Comparison of Figs. 1 and 2 indicates that adsorption of Tween 80 solutions was much lower than adsorption of SDS solutions onto mefenamic acid. The Il Yang mefenamic acid adsorbed the surfactant slightly faster than the Chimica mefenamic acid; both types reached a plateau at about 0.073% Tween 80.

As concentrations below the CMC do not wet the drug sufficiently, meaningful interpretation was not possible. Similar results are described by Luner et al. (12) for a drug designated CI-976. Contact angle measurements and adhesion tension plots of Tween 80 and SDS solutions were investigated. The data for Tween 80 showed that there was preferential adsorption of the surfactant to the liquid-vapor interface compared to the solid-liquid interface. Higher concentrations of SDS solutions with low surface tension adsorbed preferentially at the solid-liquid interface. Thus, it may be deduced that Tween 80 solutions did not completely wet the solid surface at any practical concentration, while SDS solutions reached a contact angle near zero.

Dissolution Rates

Both types of mefenamic acid were characterized by almost the same dissolution behavior (Fig. 3). The first step in the dissolution process wais the disintegration of the hard gelatin capsule, which was completed within 5

Table 1

Laser Diffraction Data and BET Surface Area Measurements of Il Yang (IY) and Chimica (CH) Mefenamic Acid

Lot	Particle Size Distribution (μm)						BET Surface Area (m^2/g)
	×10	×16	×50	×84	×90	×99	
IY 1069015	2.52	4.15	12.36	30.33	37.93	66.50	0.922
IY 1339096	2.23	5.41	17.54	41.43	50.25	79.93	0.683
IY 1340096	3.35	5.62	18.01	42.58	51.96	83.87	0.626
IY 1346116	3.34	5.60	17.89	40.84	49.14	77.90	0.712
CH 1116036	2.28	3.62	9.17	22.09	30.41	71.45	0.852
CH 1116036H	2.35	3.66	9.29	23.38	33.60	98.42	0.833
CH 1128066	2.38	3.85	10.78	33.85	45.44	79.70	0.742

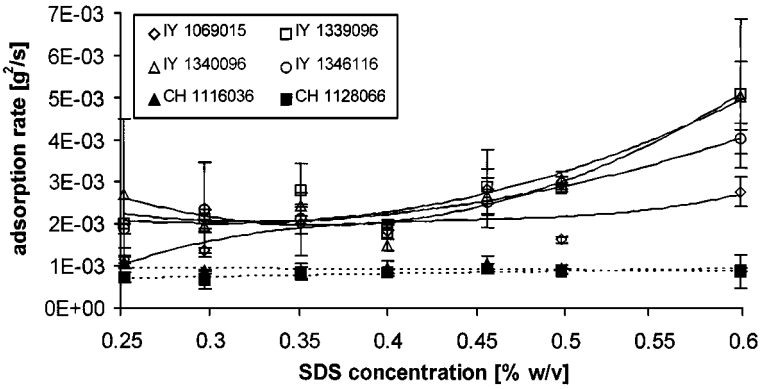

Figure 1. Adsorption rate of SDS solutions on Il Yang (IY) and Chimica (CH) mefenamic acid versus concentration of SDS.

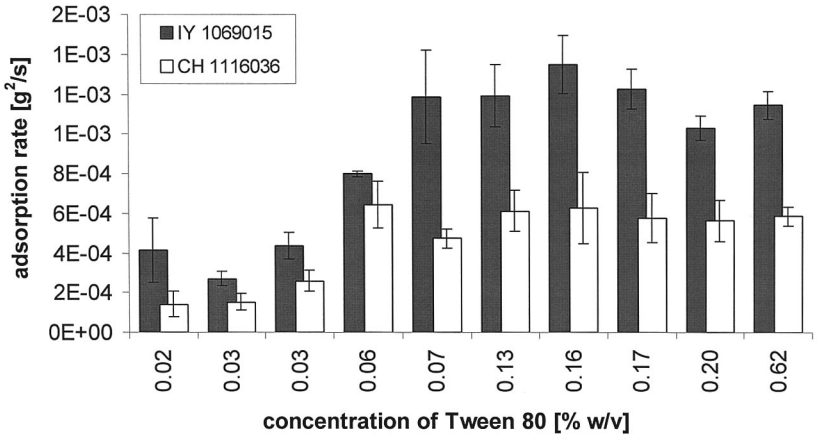

Figure 2. Adsorption rate of Tween 80 solutions on Il Yang (IY) and Chimica (CH) mefenamic acid versus concentration of Tween 80.

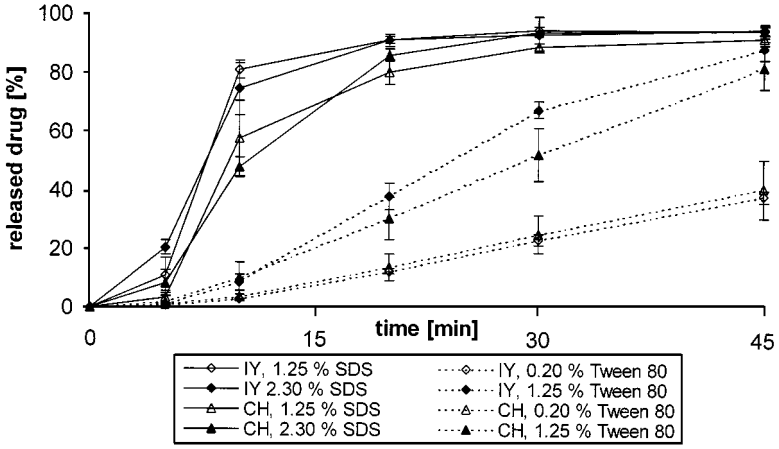

Figure 3. Dissolution rates of mefenamic acid bulk drug capsules for Il Yang (IY) lot 1069015 and Chimica (CH) lot 1116036 mefenamic acid.

min in every dissolution medium. Dissolution rates in media containing Tween 80 increased slowly and did not reach a plateau until the end of the measurement. However, the amount of drug released in 45 min increased from 35% to 75% when the concentration of Tween 80 in the medium increased from 0.2% to 1.25%. Il Yang mefenamic acid showed a slightly faster dissolution rate, but insufficient drug release. Dissolution was accelerated in media containing SDS, in which the release rates reached a plateau after 15 to 20 min in each experiment. Release rates of the Il Yang batches were slightly faster. The results confirm the results of wettability tests and indicate that SDS cannot be replaced by Tween 80 to enhance dissolution rates.

Differential Scanning Calorimetry

It is well known that mefenamic acid shows two polymorphic forms. Umeda et al. (13) described that the transition of polymorphic form I into form II takes place at 179°C. At 230°C, the polymorphic form II melts under decomposition (14). To examine whether the transition into the metastable form II was reversible and if a difference between the batches existed, the samples were first heated to 225°C and cooled. After storage for 1 week at room temperature, the samples were heated for a second time to 300°C. Figures 4 and 5 show the DSC curves of the Il Yang and Chimica batches. The data of all onset temperatures are summarized in Table 2. All DSC curves

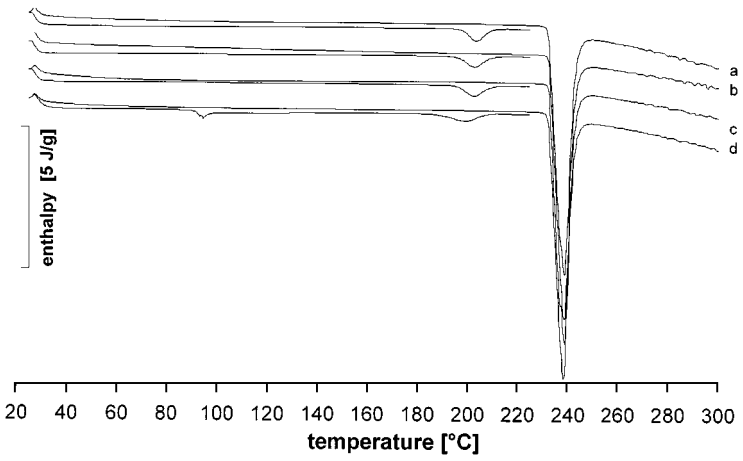

Figure 4. DSC curves of Il Yang mefenamic acid: (a) lot 1346116; (b) lot 1340096; (c) lot 1339096; and (d) lot 1069015.

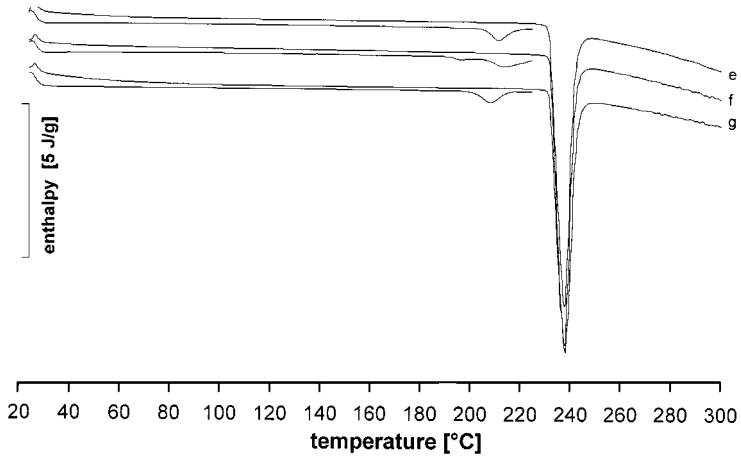

Figure 5. DSC curves of Chimica mefenamic acid: (e) lot 1128066; (f) lot 1116036; and (g) lot 1116036H.

show one endothermic peak during the first heating at onset temperatures ranging from 187°C to 205°C. These values do not agree with those in the literature (13). The onset temperature of lot 1069015 (Fig. 4) was somewhat closer to the value indicated elsewhere (13), but the peak is less sharp than the peaks of the other Il Yang batches, which had onset temperatures that show a difference of more than 15°C. The Chimica batches (Fig. 5) show even higher transition temperatures of 205°C. When the drug was pretreated with *n*-hexane, the peak becomes sharper, and the onset temperature decreased to 200°C.

During the second heating, there appears to be no difference between the batches. All curves show an endothermic peak at an onset temperature of 230°C, which is stated to be the melting point of polymorphic form II. Thus, the results of this study indicate that, during a storage period of 1 week, polymorph II was not converted into polymorph I.

Table 2

Onset Temperature of Differential Scanning Calorimetry Transition (First Peak) and Melting Points (Second Peak) of Il Yang (IY) and Chimica (CH) Mefenamic Acid

	Onset Temperature First Peak (°C)	Onset Temperature Second Peak (°C)
IY 1069015	187.52	231.29
IY 1339096	194.94	231.51
IY 1340096	195.35	231.48
IY 1346116	196.92	231.04
CH 1116036	205.63	231.18
CH 1116036H	200.82	230.95
CH 1128066	205.32	230.71

X-Ray Powder Diffraction

The X-ray powder diffraction measurements represented in Table 3 show differences between the Il Yang and Chimica batches. The *d* values and relative intensities are comparable, but there does exist one additional peak for all Chimica batches at a theta angle of 17.37 (°2θ). The *d* values and relative intensities of these peaks are almost the same, and there is no difference between pretreated and nontreated batches. One additional peak appears at a theta angle of 27.57 (°2θ) that could not be related to one type of mefenamic acid.

Scanning Electron Micrographs

The scanning electron micrographs of Il Yang mefenamic acid are presented in Fig. 6. Lot 1069015 shows needle-shaped flat particles. The smaller particles are agglomerated, and some of them adhered to the larger ones. All particles are sharp edged and seem to laminate. The particle shapes of the other Il Yang batches are not as sharp edged; the particles are no longer needles, but are flat plates with rounded edges, and they also seem to laminate. All Il Yang batches are characterized by a wide particle size distribution. Figure 7 shows SEMs of Chimica mefenamic acid. Most of the particles are small and nearly the same size; there are only a few larger particles. The particles are also needle shaped, but no plates are observed; the particles seem to laminate less than those

Table 3

X-Ray Powder Diffraction Data of Il Yang (IY) and Chimica (CH) Mefenamic Acid

	IY 1069015		IY 1339096		IY 1340096		IY 1346116		CH 1116036		CH 1116036H		CH 1128066	
Angle (°20)	*d*	I/I_0	*d*	I/I_0	*d*	I/I_0	*d*	I/I_0	*d*	I/I_0	*d*	I/I_0	*d*	I/I_0
6.33	13.86	100.0	13.80	100.0	13.92	100.0	13.70	100.0	13.76	100.0	13.79	100.0	13.78	100.0
12.69	7.01	6.1	6.97	3.9	6.97	4.0	6.93	4.7	6.93	4.1	6.94	3.8	6.93	4.1
13.89	6.39	47.1	6.34	19.3	6.37	24.7	6.35	27.7	6.36	31.4	6.36	28.0	6.37	33.6
14.25	6.20	18.2	6.21	9.0	6.19	11.4	6.15	11.5	6.15	16.7	6.15	18.6	6.18	17.8
15.09	5.86	23.2	5.84	11.3	5.88	15.1	5.83	16.6	5.84	22.0	15.16	20.2	5.85	24.3
15.81	5.60	81.3	5.57	42.8	5.65	41.7	5.56	59.8	5.56	52.6	5.57	53.4	5.56	55.7
16.89	5.26	11.2	5.24	4.9	5.25	6.3	5.25	6.5	5.24	7.1	5.24	8.5	5.23	8.4
17.37[a]	—	—	—	—	—	—	—	—	**5.09**	**2.9**	**5.09**	**2.7**	**5.10**	**3.2**
20.13	4.41	37.2	4.39	18.7	4.43	21.8	4.41	25.3	4.40	23.8	4.43	22.3	4.40	23.8
21.33	4.15	93.5	4.14	52.5	4.15	54.5	4.13	71.2	4.14	66.5	4.14	76.7	4.14	60.2
23.85	3.73	5.8	3.71	3.1	3.73	3.1	3.72	4.1	3.70	4.4	3.72	5.4	3.71	4.6
25.05	3.54	18.5	3.54	10.2	3.54	10.5	3.54	12.8	3.53	11.7	3.54	11.3	3.56	12.6
26.25	3.39	86.0	3.39	47.7	3.40	51.1	3.39	65.3	3.39	60.0	3.40	65.0	3.40	67.4
27.57[b]	—	—	**3.24**	**8.3**	**3.25**	**10.8**	—	—	**3.37**	**13.5**	**3.27**	**12.8**	**3.41**	**14.9**
27.81	3.20	24.9	3.21	10.9	3.21	12.5	3.20	16.2	3.20	17.4	3.20	17.3	3.21	17.9
30.33	2.95	6.7	2.93	3.5	2.94	3.9	2.95	4.5	2.94	4.7	2.94	4.6	2.95	4.9
31.41	2.85	14.5	2.85	6.5	2.85	7.9	2.84	9.6	2.84	10.4	2.84	8.2	2.85	10.1
32.01	2.79	15.3	2.80	7.7	2.80	8.9	2.79	11.6	2.78	9.4	2.79	8.9	2.79	9.7
32.85	2.72	5.7	2.72	2.8	2.72	3.8	2.72	4.2	2.71	4.0	2.72	4.5	2.72	4.8
40.53	40.54	9.1	2.22	5.2	2.22	6.2	2.22	7.6	2.22	5.7	2.23	5.6	2.22	6.3

[a] Bold values at a theta angle of 17.37 indicate differences between mefenamic acid Il Yang and Chimica.

[b] Bold values at a theta angle of 27.57 indicate the occurrence of additional peaks not specific for one supplier.

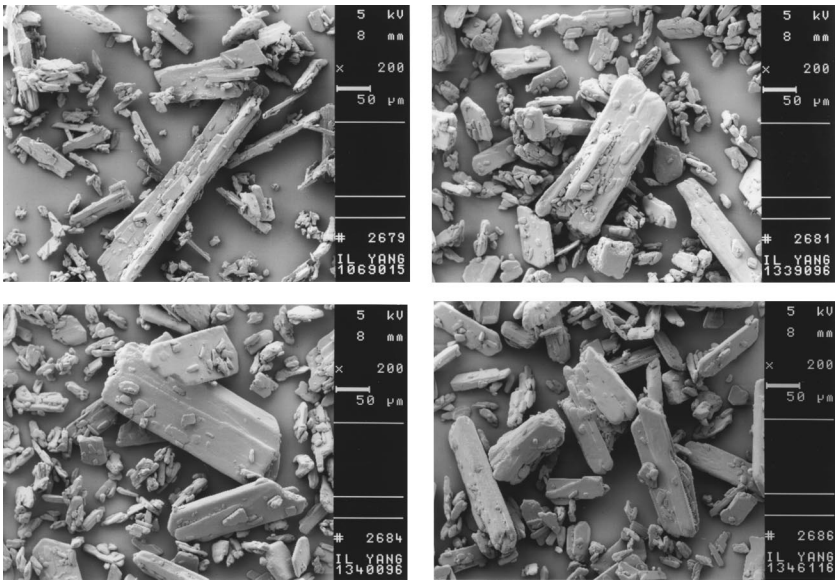

Figure 6. Scanning electron micrographs of Il Yang Metha mefenamic acid: 2679, lot 1069015; 2681, lot. 1339096; 2684, lot 1340096; and 2686, lot 1346116.

of Il Yang batches. The pretreated batch has the same crystal habit as the nontreated batches.

Force-Time Profiles

The standardized force-time profiles of mefenamic acid and Starch 1500 at 5 kN are shown in Fig. 8. The corresponding data and A6/A5 quotients are given in Table 4. The compression curves are classified into four sections: A1 defines the compression; A2 and A3 represent the first and second half of the dwell time, respectively, and give information about plastic or brittle fracture of the substance; and A4 describes the relaxation. Vogel and Schmidt (15) also classified areas A2 and A3 above the

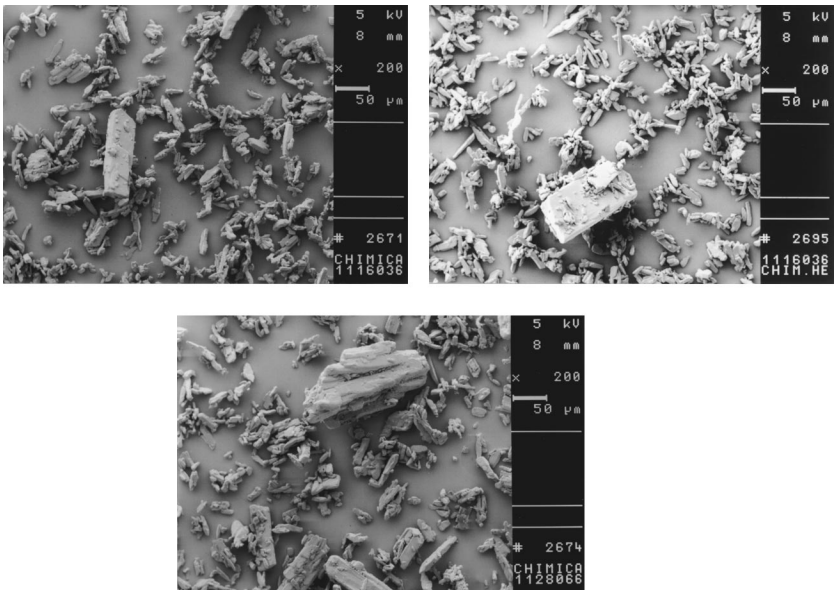

Figure 7. Scanning electron micrographs of Chimica mefenamic acid: 2671, lot 1116036; 2695, lot 1116036H; 2674, lot 1128066.

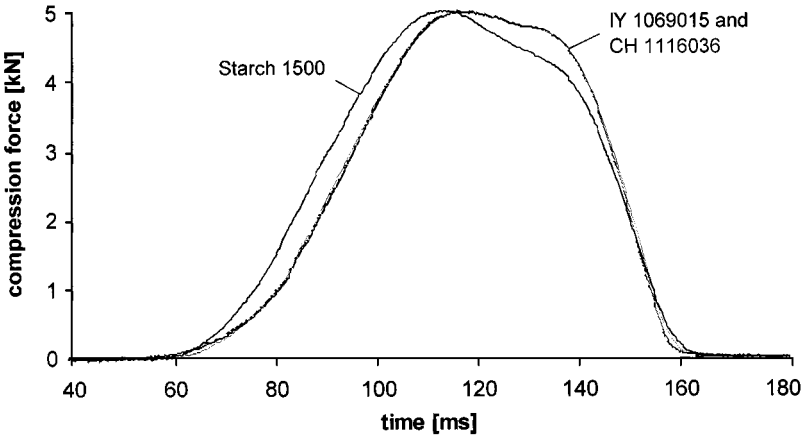

Figure 8. Force-time profiles of Il Yang lot 1069015 mefenamic acid, Chimica lot 1116036 mefenamic acid, and Starch 1500 lot 402026 standardized to a compression force level of 5 kN.

minimum compression force of the dwell time and obtained areas A5 and A6. The area quotient A6/A5 can provide information about plastic or brittle deformation under compression and exclusively depends on the powder properties. Substances with mainly plastic behavior have low A6/A5 quotients between 0.3 and 0.45 at low compression forces and a steep slope at increasing compression forces. Substances with brittle behavior, on the other hand, have A6/A5 quotients above 0.6 at low compression forces and a less steep slope at higher compression forces. Both types of mefenamic acid showed the same compression behavior; the differences in their physicochemical properties described above had no influence on compression. The A6/A5 quotient of approximately 0.7 shows that the substance undergoes brittle deformation. Compared to Starch 1500, the elastic components are less marked.

CONCLUSION

The two manufacturers of mefenamic acid produced substances with varying properties. Due to the smaller particle size, the Chimica batches were characterized by a higher sticking tendency and higher hydrophobicity. This was manifested by the lower degree of wettability and problems in granulation and dissolution. For both types of mefenamic acid, SDS was a better surface-active agent to enhance wettability and dissolution rates. Due to similar force-time curves of the different types of mefenamic acid and better properties concerning wettability and the granulation process, the Il Yang lot 1069015 was used for further investigations, which will be described in a future paper. The present study signifies that the exact physicochemical characterization of a drug can help in the choice of the best starting material for the develop-

Table 4

Area Data and A6/A5 Quotients of Force-Time Profiles of Il Yang Mefenamic Acid Lot 1069015, Chimica Mefenamic Acid Lot 1116036, and Starch 1500 Lot 402026

	Weight (mg)	F_{max} (kN)	A1	A2	A3	A4	A5	A6	A6/A5
Starch 1500	239.5	5.22	99,630	95,236	77,385	16,835	42,027	24,176	0.575
M. Il Yang	221.4	5.148	79,008	94,742	83,270	15,324	38,817	27,344	0.704
M. Chimica	219.6	5.521	85,673	101,583	89,660	18,571	39,318	27,394	0.697
Starch 1500	287.4	10.33	228,633	190,229	163,526	54,589	65,471	38,768	0.592
M. Il Yang	257.0	10.25	166,951	187,488	172,462	55,839	53,447	38,422	0.719
M. Chimica	243.7	10.43	175,673	191,004	174,892	58,103	54,926	38,814	0.707

ment of an optimum dosage form and to economize processes involved.

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