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Morphic features variation of solid particles after size reduction: sonification compared to jet mill grinding

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Summary

Fourier descriptors of the contour were used to evaluate the effect of sonification and jet mill grinding on particle shape. While jet mill grinding produced particles with smoother boundary, less elongation and higher degree of roundness, sonification yielded fragments closer in shape to the original crystal. Data obtained suggest that the morphic features of daughter fragments are determined mainly by the mechanism of size reduction and material structure.

Introduction

Size reduction is used to produce small particle size of active ingredients to assure a maximum surface area for solubilization and bioavailability (Boullay, 1985). Much work has been done over the years for evaluating particle size reduction, the mechanism of comminution and variables operating in this process (Parrot, 1974; Austin, 1984).

Sonification has been used in phase dispersion of emulsions (Guay and Bisaillon, 1979), deaggregation of solid particles in suspensions and in accelerating the dissolution of poorly soluble par-

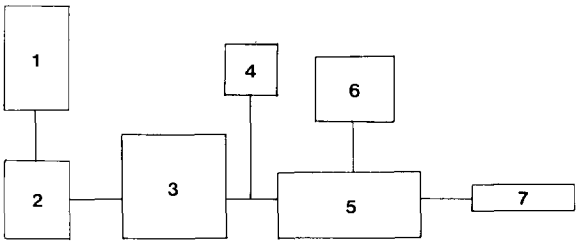

Fig. 1. Schematic diagram of the image analysis system: 1, Zeiss light microscope; 2, Sony CCD video camera; 3, Matrox color monitor; 4, Matrox digitizer; 5, IBM-AT; 6, Amdek monitor; 7, Epson printer.

TABLE 1

Size and shape parameters of salbutamol crystals before and after size reduction

Size–shape parameters	Salbutamol original crystals	Salbutamol after sonification	Salbutamol after micronization
Diameter (μm)	52.32 ± 21.56	5.83 ± 1.76	0.91 ± 0.32
Roundness (P1)	0.53 ± 0.05	0.64 ± 0.05	0.68 ± 0.05
Elongation (P2)	0.40 ± 0.14	0.68 ± 0.16	0.73 ± 0.13

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ticles (Beaubien and Vanderwielen, 1980). Size reduction of charcoal (Robinson, 1985), minerals (Parekh et al., 1984) and renal calculi (Marberger, 1983) using ultrasonics has been documented in different studies. There is no specific reference in these studies to the effect of sonification on the morphic features of the resulting solid particle.

In a recent communication, using Fourier descriptors of the contour, we found that micronization of salbutamol crystals by jet mill resulted in particles with smoother boundaries, less elongation and higher degree of roundness (Akbarieh and Tawashi, 1987). The purpose of this work is to demonstrate the effect of sonification on particle morphology, to compare data obtained in jet mill grinding with sonification and to develop a relation between the shape of the fragments produced and the mechanism of their formation.

Materials and Methods

In this study we used salbutamol base [1] (B.P.), a crystalline powder, used as a bronchodilator. The crystals were subjected to a Sonifier Cell Disruptor (Model W-140D) [2] with a frequency of 20 kHz and intensity of the ultrasonic field of approximately 125 W/cm^2. The head of the horn was totally immersed in a suspension containing 0.05% salbutamol crystals in kerosene [3]. The temperature was controlled using a cooling water bath. Samples were taken at regular intervals and a series of scanning electron micrographs [4] were

[1] Glaxo Laboratories, Toronto, Ontario, Canada.
[2] Heat Systems-Ultrasonics Inc., Farmingdale, NY, U.S.A.
[3] Fisher Scientific, Fair Lawn, NY, U.S.A.
[4] SEM-Jeol, ISM 840, Tokyo, Japan.

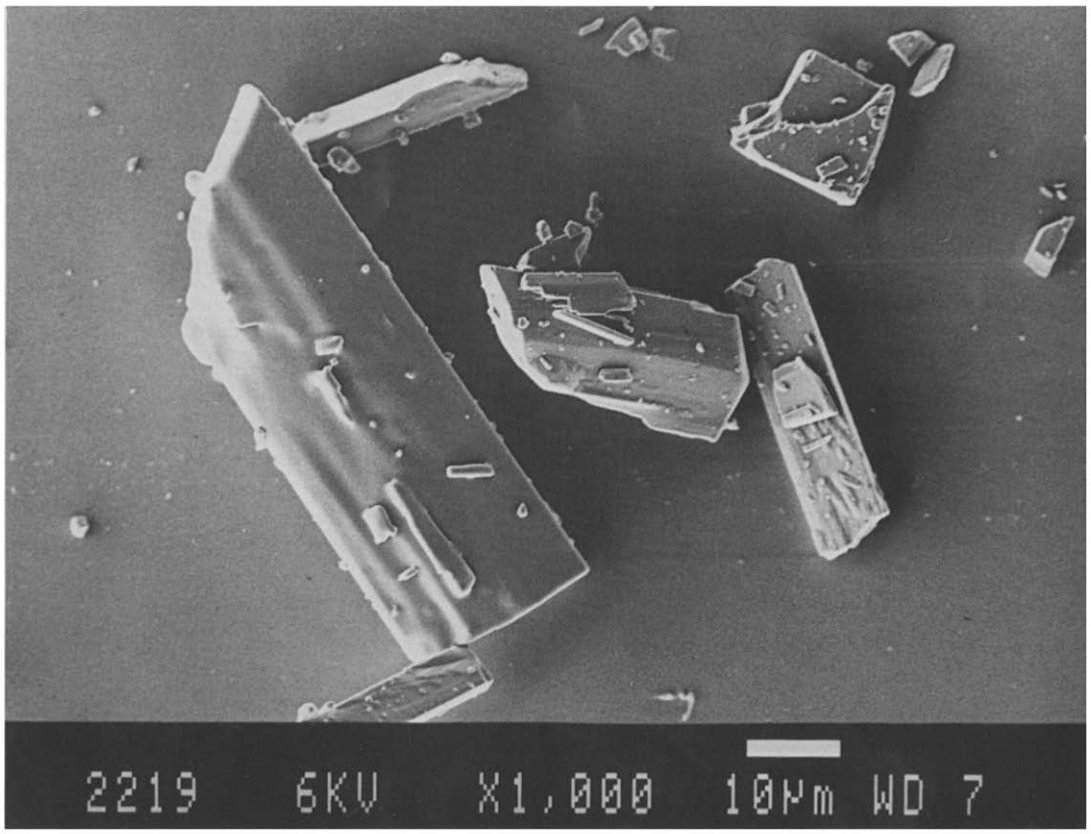

Fig. 2. Scanning electron micrograph of salbutamol crystals before size reduction.

prepared for the original crystals, and for those obtained after sonification. A laboratory jet mill (Trost Mill, type 1047, Garlock Inc., Newtown, PA) operated at 100 psi with dry air was used. Size and shape characteristics were determined using a modified image analysis system which has been previously described (Akbarieh et al., 1987). In this study at least 100 individual crystals were analysed in each run and aggregates were not considered.

Fig. 1 shows a diagram of the system used for digitizing and extracting shape features from the scanning electron micrographs. The configuration of the system is as follows: a Zeiss light microscope; a Sony CCD video camera (AVC-D1); a color monitor (Model C-3419CLP/WC, resolution 512*512, Matrox); a PIP-512/1024A digitor (Matrox); an IBM-AT unit; an Amdek monitor (Video-300A) and an Epson printer (FX-85).

Using Fourier descriptors which are based on the digitization of the particle image, the (x, y) coordinates of the particle boundary were extracted. These coordinates were used to calculate a set of invariant shape descriptors. The details of this method have been described in a previous communication (Akbarieh and Tawashi, 1987; Dubuc et al., 1987).

Results and Discussion

Fig. 2 shows the original salbutamol crystals before size reduction. It appears clearly from the SEM micrograph that the original crystals are elongated with sharp corners and edges. The sonification of salbutamol crystals produced fragments approximately 10 times smaller in size (Fig. 3). These particles still possess edges and distinct corners and look different in shape from the salbutamol crystals micronized by fluid energy mill (Fig. 4). Individual fragments appear relatively rounder and smoother than the original particles, because of the loss of some edges and corners. Sonified particles have better flow properties. Jet-milled particles tend to aggregate and to

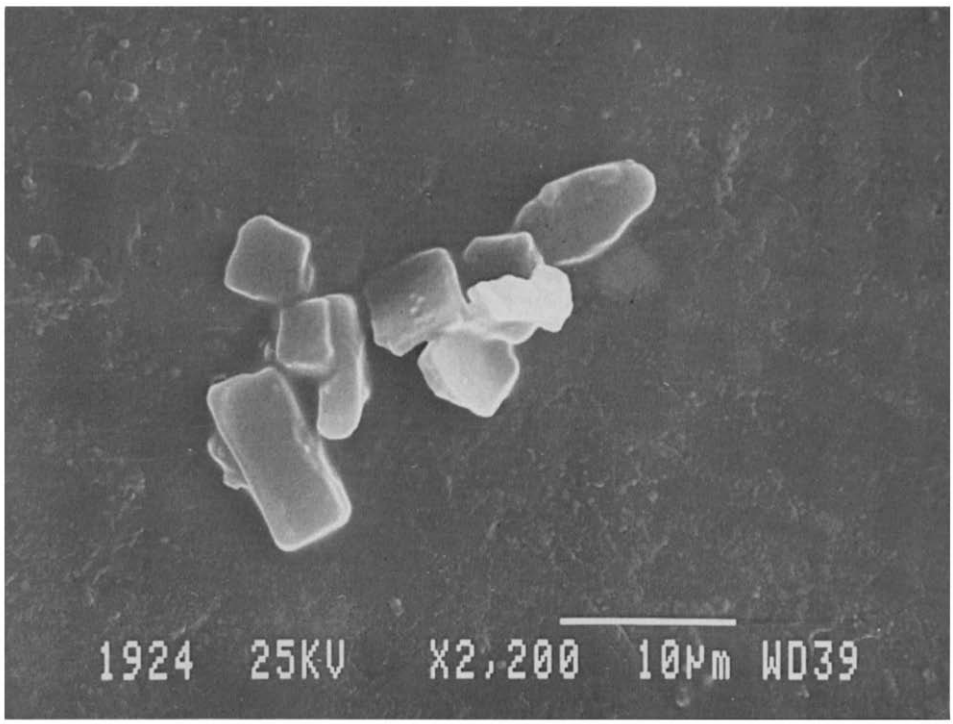

Fig. 3. Scanning electron micrograph of salbutamol fragments after 10 min of sonification.

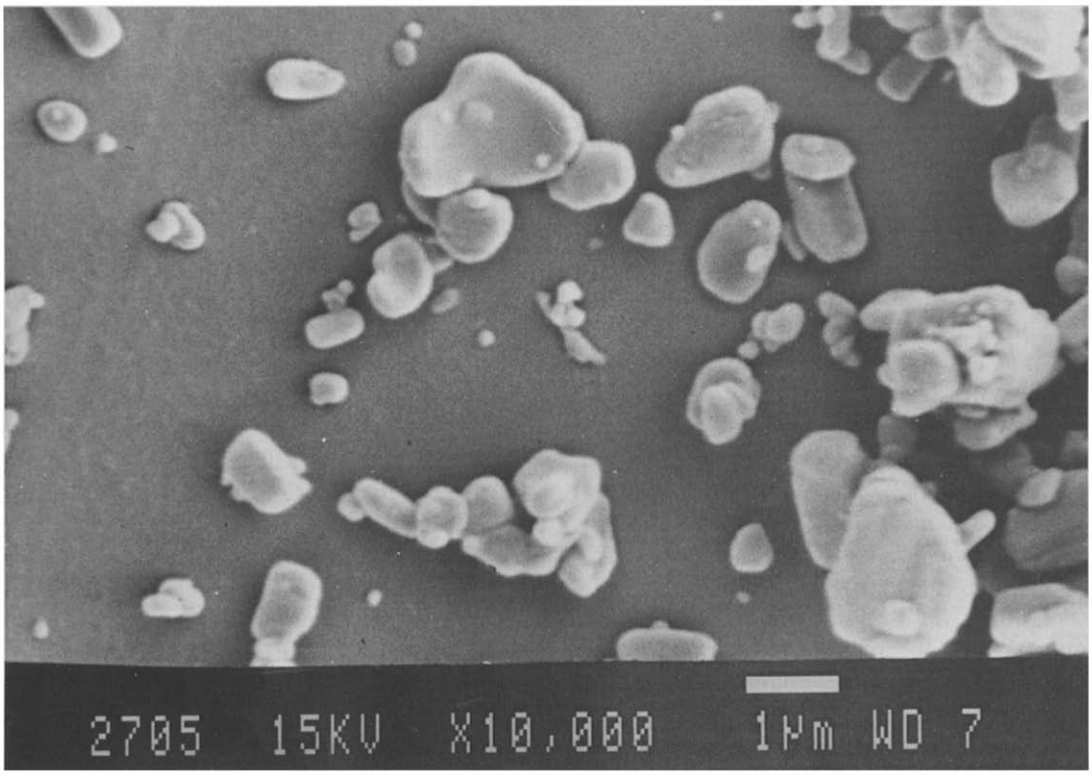

Fig. 4. Scanning electron micrograph of salbutamol fragments after jet mill grinding.

adhere to solid surfaces more than sonified particles.

The morphological analysis of salbutamol crystals before and after size reduction is given in Fig. 5. The shape spectrum shows clearly the influence of both sonification and jet grinding on particle shape. From the average normalized Fourier amplitudes it appears that the daughter fragments produced by sonification are closer in shape to the original crystal, than the jet-milled particles.

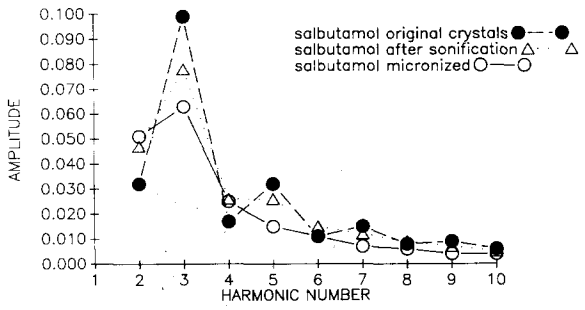

Fig. 5. Amplitude spectra. The amplitude vs harmonic number for salbutamol crystals before and after size reduction.

The size and shape features of the starting material and the milled particles are summarized in Table I. Sonification of the salbutamol crystals for 10 min reduced the particle size to an average size of 6 μm; however, the fluid energy mill reduced the particle size to nearly 1 μm.

Fig. 6 shows that the frequency of roundness (P1) obtained in the two processes as compared with the original crystals. P1 is closer to 1 in micronized crystals than the case of sonification and the original material. Elongation (P2) is a measure of the ratio between the long axis and the short axis of the fitted ellipse. The examination of the frequency of elongation (Fig. 7) indicates that the P2 is closer to zero for the particles produced by sonification than the micronized fragments resulted from jet mill grinding.

These findings suggest that in jet mill grinding, collision between the fractured particles and be-

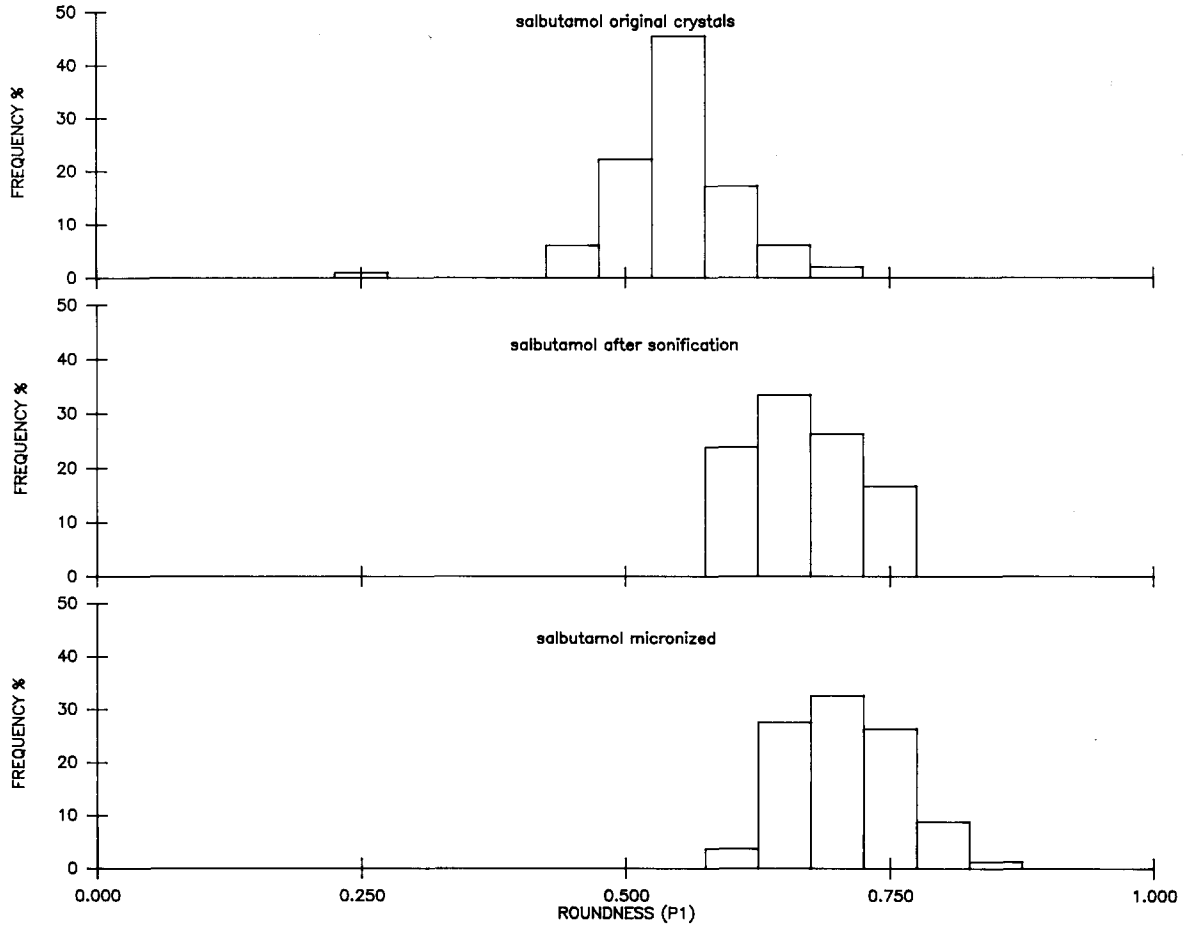

Fig. 6. Roundness (P1) frequency distribution of salbutamol crystals before and after size reduction.

tween the particles and the walls of the jet mill reduced the corners and edges of the fragments. The observed final fragments were smooth and round because of the loss of corners and edges by abrasion. Their disappearance can be attributed to the higher surface energy of these sites.

In the case of sonification, the particles obtained were less round and possess relatively sharper edges. This can be explained on the basis of the nature of the acoustic energy involved in size reduction and the microstructure of the salbutamol crystals.

As most crystals, salbutamol crystals contain imperfections like microcracks and dislocations. During sonification the acoustic waves apparently activated the gas bodies which are located in the microcracks leading to cavitation bubbles (Neppiras, 1984). The growth of cavitation within the solid, by the ultrasonically generated compressed–decompressed wave-train, leads to crack propagation along the weak dislocation lines (Fridman, 1972; Sarfarazi and Ghosh, 1987). The sudden release of pressure resulted in fracture and shattering. The final fragments obtained displayed morphological features closer to the original crystal than the micronized crystals. Their relatively rounded corners can be attributed to mechanical wear and/or attrition produced by the acoustical field. Thus, these experiments demonstrate clearly that the shape parameters of the fragments of

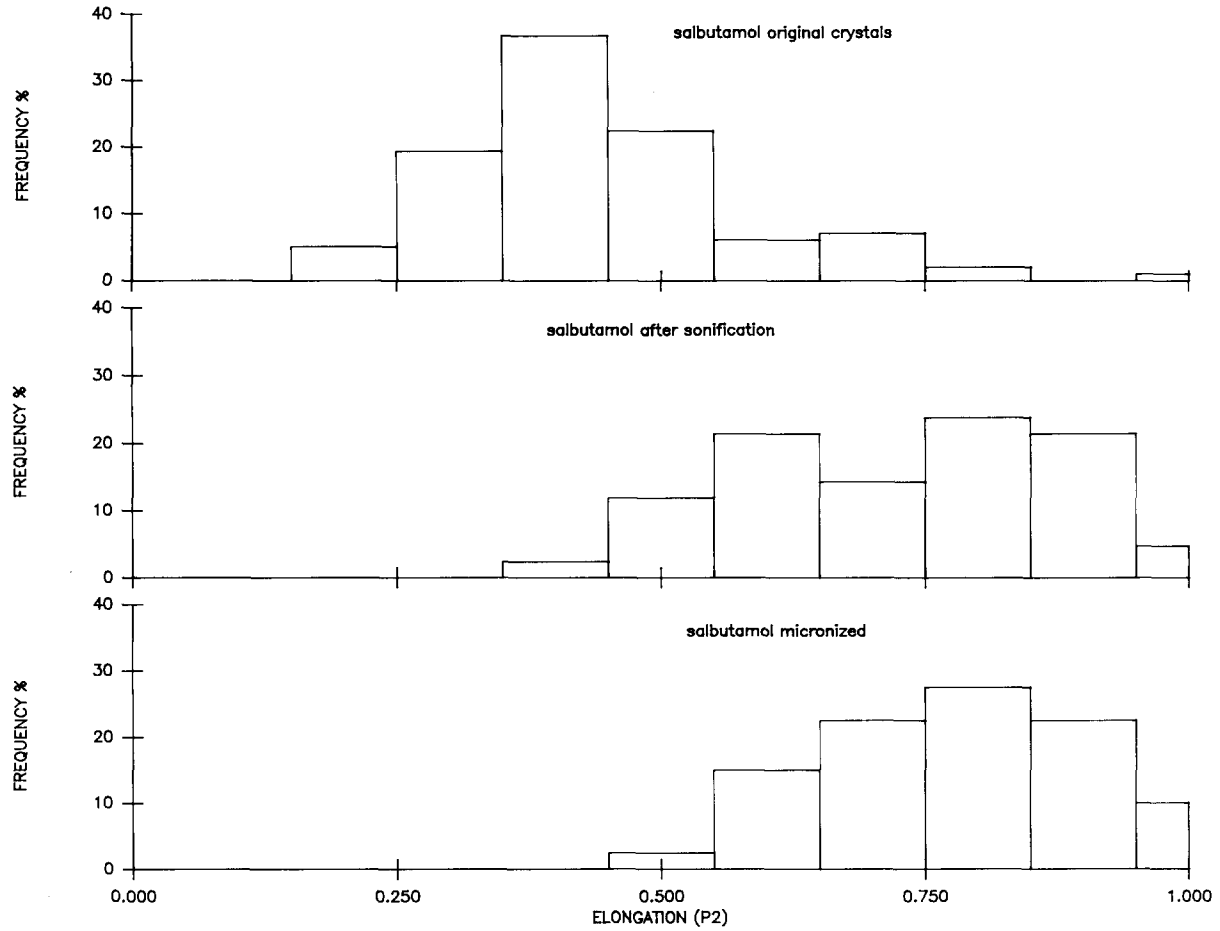

Fig. 7. Elongation (P2) frequency distribution of salbutamol crystals before and after size reduction.

particulate solids obtained after jet-milling and sonification are mainly determined by the mechanism operating in grinding and the internal structure of the material.

Acknowledgements

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References

Akbarieh, M and Tawashi, R., Morphic features of solid particles after micronization in the fluid energy mill. *Int. J. Pharm.*, 35 (1987) 81–89.

Akbarieh, M., Dubuc, B. and Tawashi, R., Surface studies of calcium oxalate dihydrate single crystals during dissolution in the presence of urine. *Scanning Microsc.*, 1 (1987) 1397–1403.

Austin, L.G., Size reduction of solids: crushing and grinding equipment. In Fayed, M.E. and Otten, L. (Eds.), *Handbook of Powder Science and Technology*, VNR, New York, 1984, p. 578.

Beaubien, L.J. and Vanderwielen, A.J., Particle size analysis of pharmaceutical powders. *J. Pharm. Sci.*, 69 (1980) 651–655.

Boullay, G. Microbroyage et dissolution. *STP Pharma.*, 1 (1985) 296–299.

Dubuc, B., Piché, J., Darveau, R. and Tawashi, R. Des descripteurs de contour de particules solides appliqués à l'étude de systèmes pharmaceutiques. *Pharm. Acta Helv.*, 62 (1987) 81–87.

Fridman, V.M. The interaction mechanism between cavitation bubbles and particles of the solid and liquid phases. *Ultrasonics*, 10 (1972) 162–165.

Guay, F. and Bisaillon, S., Evaluation of fat emulsions prepared by ultrasonic waves. *Drug Dev. Ind. Pharm.*, 5 (1979) 107–126.

Marberger, M., Disintegration of renal and ureteral calculi with ultrasound. *Urol. Clin. North Am.*, 10 (1983) 729–742.

Neppiras, E.A., Acoustic cavitation: an introduction. *Ultrasonics*, 22 (1984) 25–28.

Parekh, B.K., Epstein, H.E. and Goldberger, W.M., Novel comminution process uses electric and ultrasonic energy. *Min. Eng.*, 36 (1984) 1305–1309.

Parrot, E.L., Milling of pharmaceutical solids. *J. Pharm. Sci.*, 63 (1974) 813–829.

Robinson, P.D., Ultrasonic vs. mechanical comminution of coal II. Annual Report July 1, 1984–June 30, 1985, U.S. Department of Energy, 1985 p. 20.

Sarfarazi, M. and Ghosh, S.K., On the micromechanical theories of stress-induced cleavage microcracking in crystalline solids. *Engng. Fracture Mech.*, 27 (1987) 215–230.