Available online at www.sciencedirect.com
ScienceDirect
Ultrasonics Sonochemistry 14 (2007) 717–724
Ultrasonics SONOCHEMISTRY
www.elsevier.com/locate/ultsonch

Ultrasound-assisted crystallization (sonocrystallization)

M.D. Luque de Castro *, F. Priego-Capote

Department of Analytical Chemistry, Annex Marie Curie Building, Campus of Rabanales, University of Córdoba, Córdoba, Spain

Received 17 September 2006; received in revised form 5 December 2006; accepted 6 December 2006
Available online 24 January 2007

Abstract

The positive influence of ultrasound (US) on crystallization processes is shown by the dramatic reduction of the induction period, supersaturation conditions and metastable zone width. Manipulation of this influence can be achieved by changing US-related variables such as frequency, intensity, power and even geometrical characteristics of the ultrasonic device (*e.g.* horn type size). The volume of the sonicated solution and irradiation time are also variables to be optimized in a case-by-case basis as the mechanisms of US action on crystallization remain to be established. Nevertheless, the results obtained so far make foreseeable that crystal size distribution, and even crystal shape, can be 'tailored' by appropriate selection of the sonication conditions.

PACS: 43

Keywords: Crystallization; Ultrasound; Induction period; Supersaturation; Metastable zone width

1. Introduction

Crystallization is a process used in many industrial domains including chemical, pharmaceutical and petrochemical industries, and usually considered in terms of nucleation and crystal growth [1]. Nucleation processes – *viz.* production of microscopic crystals – are classified in Fig. 1. So called "primary nucleation" occurs when a crystal is nucleated in a solution containing no pre-existing crystals. On the other hand, nucleation induced in the bulk of a liquid in the absence of solid surfaces is called "homogeneous nucleation". If a solid interface – whether a container wall or a pre-existent crystal – is involved, the process is called "heterogeneous nucleation". Finally, nucleation induced by pre-existing crystals is called "secondary nucleation" and results from the crystals either acting as templates for new crystal nuclei or fragmenting to produce more nucleation sites. Although nucleation theories have advanced considerably in recent years, the templating or a particular ordering within the solid state *via* the nucleation process is not fully understood [2].

True homogeneous nucleation is uncommon in practice, and only happens at high levels of supersaturation. Under such high levels, reversible clustering occurs. Beyond the clustering stage, it appears that a point is reached in the development of order and consolidation at which the cluster is able to "template" further accretion of material into the solid matrix, and a nucleus can be considered to have formed. Although it is not possible to theoretically characterize the transition from a cluster to nucleus, it is probably a continuation of the dynamic process by which clusters originally form as spatial inhomogeneities in the supersaturated solution.

In practice, nucleation almost always occurs heterogeneously, and in theoretically clean and particle-free solutions it is believed to be associated with spurious traces of suspended material or imperfections in the container's surfaces that function as nucleation sites; thus, it is not surprising that the reproducibility of nucleation in these systems is very poor. The lack of a theoretical understanding

* Corresponding author. Tel./fax: +34 957 218615.
E-mail address: qa1lucam@uco.es (M.D. Luque de Castro).

1350-4177/$ - see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.ultsonch.2006.12.004

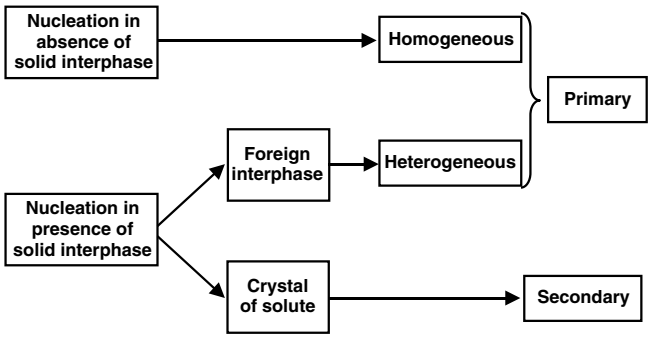

Fig. 1. Classification of nucleation processes.

of homogeneous nucleation makes it difficult to predict what the effects of ultrasound (US) will be, and whether consideration of primary nucleation is relevant in interpreting the results.

2. Characteristics of sonocrystallization

Research into the influence of US on crystallization processes conducted over the last 70 years has revealed that the nucleation of solid crystals from a number of liquids ranging from organic fluids to metals is affected by the presence of US waves.

There is reliable evidence that applying US not only induces nucleation, but also increases reproducibility; however, the precise mechanisms for US action on crystallization remain to be established. In fact, US can induce primary nucleation in nominally particle-free solutions and, noteworthy, at much lower supersaturation levels than would otherwise be the case. Another effect of US on nucleation is shortening the induction time between the establishment of supersaturation and the onset of nucleation and crystallization.

In addition to the highly spatially resolved regions of extreme excitation, temperature and pressure created by bubble collapse and concomitant release of shock waves, other postulates suggest that, (i) subsequent rapid local cooling rates, calculated at 10^7–10^{10} K/s, play a significant role in increasing supersaturation; (ii) localized pressure increases reduce the crystallization temperature; and (iii) the cavitation events allow the excitation energy barriers associated with nucleation to be surmounted, in which case it should be possible to correlate the number of cavitation and nucleation events in a quantitative way. There is clearly a need for further research on the relationship between cavitation and nucleation. Interestingly, it has been suggested that nucleation caused by scratching the walls of a vessel containing a supersaturated solution with a glass rod spatula could be the result of cavitation [1].

Sonocrystallization exhibits a number of features specific to the US wave that clearly distinguish it from crystallization in its absence. For most materials, such features include, (a) faster primary nucleation, which is fairly uniform thorough the sonicated volume; (b) relatively easy nucleation in materials which are usually difficult to nucleate otherwise; (c) the initiation of secondary nucleation; and (d) the production of smaller, purer crystals that are more uniform in size.

Ultrasound has been shown to significantly influence the reduction of agglomeration under given conditions. Three US effects may contribute to this phenomenon. Thus, the shock wave, which is caused by cavitation, can shorten contact between crystals to an extent precluding their bonding together. Also, some agglomeration invariably occurs at the nucleation stage. Nuclei possess a high surface area to volume ratio; this results in a high surface tension which nuclei tend to lower by adhering to one another. The surface tension decreases as crystals grow larger and become more stable, which hinder agglomeration. Finally, the excellent mixing conditions created by US also reduce agglomeration through control of the local nucleus population.

3. Effects of ultrasound on crystallization

Both types of US effects (namely, physical, which facilitate mixing-homogenization, and chemical, resulting from radical formation through cavitation) influence crystallization by altering the principal variables involved in this physical process (namely, induction period, supersaturation concentration and metastable zone width). These effects vary in strength with the nature of the US source and its location; also, their influence is a function of the particular medium to which this form of energy is applied.

3.1. Induction period and supersaturation conditions

This parameter (t_{ind}) is defined as the time elapsed between the creation of supersaturation and the appearance of crystals, and decreases as supersaturation increases. Mathematical equations for the induction time that hold for all nuclei forming and growing in a saturated solution have been reported [3]. One of the ways to determined the induction time is from conductivity measurements. Thus, formation of crystals is signaled by a drop in the solution conductivity. The crystallization time is taken to be the time where the derivative of the conductivity with respect to time becomes negative.

The induction time is dramatically reduced by the presence of US; the effect, however, depends on the particular medium and working conditions. Thus, at an absolute supersaturation of 0.0156 g K_2SO_4/g water, the induction time in the absence and presence of US was found to be 9000 and 1000 s, respectively. Also, the conductivity decreased faster with US than without US. Because the conductivity was proportional to the potassium sulphate concentration, this difference suggests that more crystalline matter was formed in the presence of US [4].

The effect of US on t_{ind} is especially significant at low absolute supersaturations; thus, contradictory results have been obtained for highly supersaturated solutions [5].

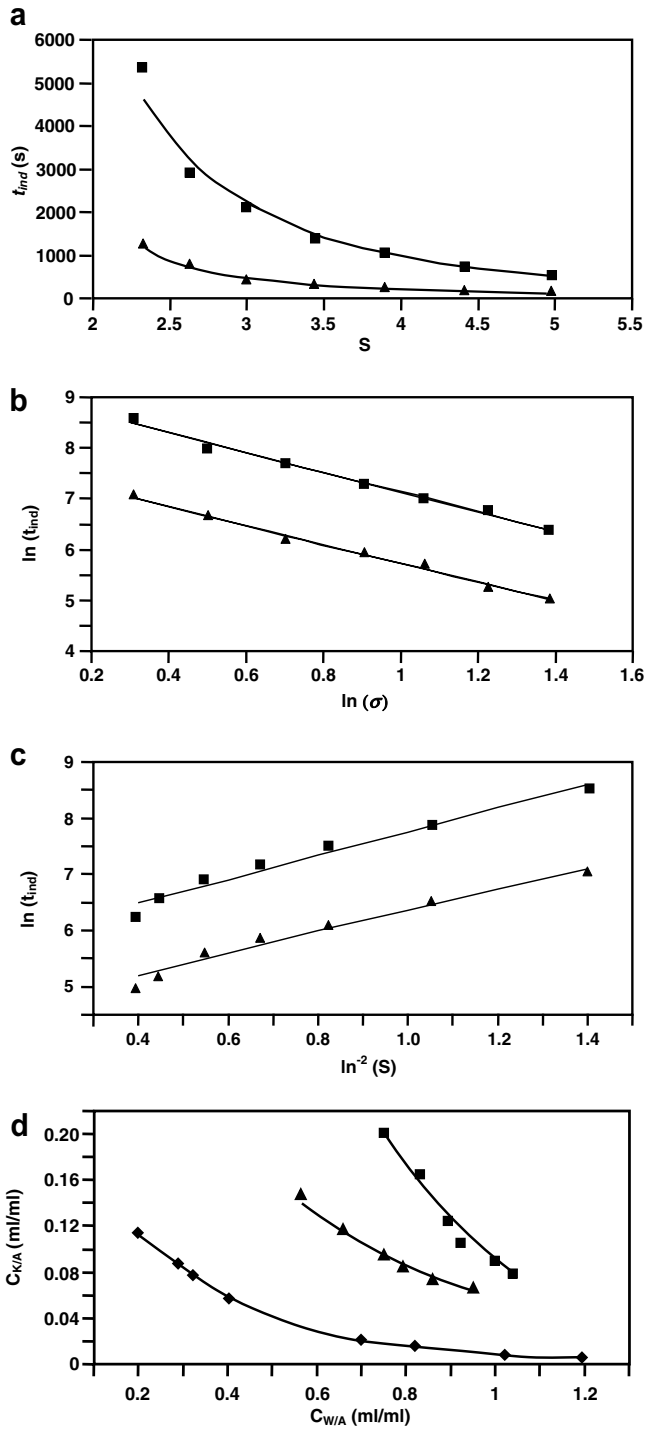

Fig. 2. Effect of US on filtration parameters. (a) Influence of US on the induction period of roxithromycin. (b) Variation of the induction time as a function of the relative supersolubility. (c) Variation of the induction time as a function of the supersaturation ratio. (d) Effect of US on the metastable zone of roxithromycin. (▲) with US, (■) without US, (♦) solubility curve (reproduced with permission of Elsevier, Ref. [6]).

Fig. 2 illustrates the effects for the anti-solvent crystallization of roxithromycin in an acetone–water mixture [6]. As can be seen in Fig. 2a the induction time decreased as supersaturation increased, whether or not US was applied. However, US significantly reduces the induction time, particularly at low supersaturations. Therefore, the effect of US on nucleation is stronger than that of high supersaturation levels [7].

Fig. 2b shows the variation of $\ln(t_{ind})$ with $\ln(\sigma)$ (σ being relative supersolubility) in the presence and absence of US. The slope and intercept of the straight line obtained with US were 2.01 and 9.04, respectively, and those obtained in its absence 1.95 and 7.59. The apparent nucleation orders were very similar and suggestive of a diffusion-controlled mechanism. The nucleation constant (k_N) was increased 4.25 times by US as a result of the significantly increased nucleation. Although the shortening of the induction time by US has been ascribed to a wall temperature effect, it results largely from the strong specific effect of US on nucleation [4].

Fig. 2c shows the linear relationship between $\ln(t_{ind})$ and $\ln^{-2}(S)$ (S being the supersaturation ratio), consistent with the typical results for crystallization processes. As can be seen, the slopes are high; the supersaturation ratio is relatively high and the lines exhibit no inflection points. This suggests the prevalence of homogeneous nucleation. The temperature at which absolute supersaturation (calculated as the difference between the actual concentration and the saturation concentration) occurs is also influenced by US. In the previous experiment, the maximum cooling time in the absence of US, about 900 s, shortened to 450 s in the presence of US.

3.2. Metastable zone width

The metastable zone width (MZW) can also be reduced by application of US. The apparent order of nucleation or growth is decreased by US. Based on available evidence, the metastable zone width can be reduced simply by applying a low US power. Thus, US decreases the apparent order of the primary nucleation rate and increases the rate of appearance of the solid. Seemingly, US modifies the mechanism of nucleation itself as its presence strongly reduces the apparent order of nucleation.

The fact that US decreases the supersaturation limit has been ascribed to its raising of the nucleation temperature. Thus, during nucleation, the cooling rate remains roughly constant; under silent conditions, however, a temperature rise is observed. After nucleation, the cooling rate decreases as the US power is raised. Two opposing effects are involved, namely: cooling is decelerated by the crystallization heat, but heat exchange is improved.

Ultrasound can induce nucleation under conditions where spontaneous primary nucleation cannot occur in its absence, thus avoiding seeding and hence the introduction of foreign particles into the solution.

In many respects, the ease or difficulty of carrying out a crystallization process can be linked to an understanding of the metastable zone (MZ). For a cooling crystallization, the MZW can be described as the temperature drop below the solubility curve at which the solid starts to separate

spontaneously for a given supersaturation level and cooling rate (supersolubility limit).

Fig. 2d shows the effect of US on the metastable zone of roxithromycin [6]. As can be seen, US significantly reduces the MZW; therefore, a supersaturated solution is much more unstable under a US field.

4. Ultrasound-related variables and their effects on crystallization

The contradictory effects of US-related variables on crystallization occasionally reported can be ascribed to considerable differences in working conditions and the nature of the systems under study.

4.1. Effect of US frequency

The ultrasound typically used in common crystallization media (mainly aqueous media) falls in the low-frequency range.

Low-frequency US waves of variable frequency (namely, 15, 20, 25 and 30 kHz) used for sonocrystallization were found to result in no substantial differences in shape, mean size or size distribution in the resulting crystals. Therefore, these wavelengths seem to have the same influence on nucleation and crystal growth. One possible explanation is that they are much larger than the size of the nuclei and crystals [8].

High-frequency US have been used to assist crystallization around the glass transition temperature for metallic glass; dramatic effect has been found which has been ascribed to rapid crystallization caused by a stochastic resonance in which the jump frequency of atoms matches the frequency of the interatomic potential change by the US vibration [9].

4.2. Effect of US intensity, power and horn tip size

Increasing the *US intensity* and *diameter of the horn tip* increases the crystallization rate. Fig. 3 illustrates the individual and combined effects of these variables in the crystallization of calcium carbonate at different US intensities and horn tip diameters of 3, 14 and 22 mm. As can be seen in Fig. 3a, increasing the US intensity decreased the Ca^{2+} concentration in the medium and increased the amount of crystallized matter formed. A similar effect was observed by increasing the diameter of the horn tip or the product of the US intensity and the square root of the horn tip area, which additionally increased the crystallization rate (see Fig. 3b and c). These two effects physically contribute to the liquid flow patterns in the reaction vessel. An increase in US intensity is expected to result in heavier flow, while one in horn tip diameter should lead to more uniform flow patterns. From these patterns, it can be concluded that the effect of cavitation known as ''microstreaming'' contributes little to crystallization, which it is more markedly affected by macrostreaming [7].

As can be seen in Fig. 3d for crystallization of hydroxyapatite (HAp), increasing the *US power* decreases the particle size [10]. No HAp crystals formed above 300 W; below this threshold, however, the particle size of the crystals formed increased with decreasing US power. Therefore, the particle size of the crystal can be controlled through the US power applied. With other inorganic crystals, and also with organic ones, raising the US power produces shorter, thicker crystals; this can be ascribed to mass transfer in the mixture being effectively accelerated and the driving force of crystallization – the driving force excepted – increased as a result. With large kinetic energies and speeds, the solute molecules will have an increased opportunity to collide with each other, penetrate the stagnant film and hence insert themselves into the crystal lattice more uniformly and easily. As the shape of the crystal depends on the growth rate at each face of the crystal, one may assume that the speed of insonated molecules is fast enough for them to approach each side of the crystal to compensate partly for differences in growth rate on each side in conventional crystallization, where diffusion control may occur. If so, one can expect a crystal insonated with a larger energy to be shorter and thicker [11]. In this way, sonocrystallization provides a method for obtaining small crystals similar to supercritical fluid micronization, but with lower equipment costs and the ability to operate under ambient conditions.

The effect of US power on formed crystals was studied at 0, 10 and 100 W by suspending potash alum crystals in a potash alum saturated solution for 3 h. Conductivity measurements showed that there was neither dissolution nor crystallization, but electron scanning microscopy revealed that the shape of the crystals changed due to erosion. Also, crystal size decreased with increasing US power. Size analysis confirmed the appearance of small particles upon application of US. The amount of smaller crystals formed was modest at a low power (10 W) but increased dramatically with increasing US power; an abrasion effect was therefore clearly involved [12].

4.3. Effect of horn immersion depth

With a US homogenizer, the flow pattern of the liquid depends on the distance from the horn tip. Since flow pattern (mixing) is the physical effect of US irradiation, any change in the flow pattern due to horn immersion may affect the crystallization rate. There is a specific horn immersion depth for each US device and irradiated medium which must be established experimentally on a case-by-case basis [7].

4.4. Effect of the volume of ultrasonicated solution

The mean crystal size is known to increase with increasing the volume of the ultrasonicated mixture. One explanation for this behavior is that a fixed US wave in a larger container produces weaker penetrating and reflecting

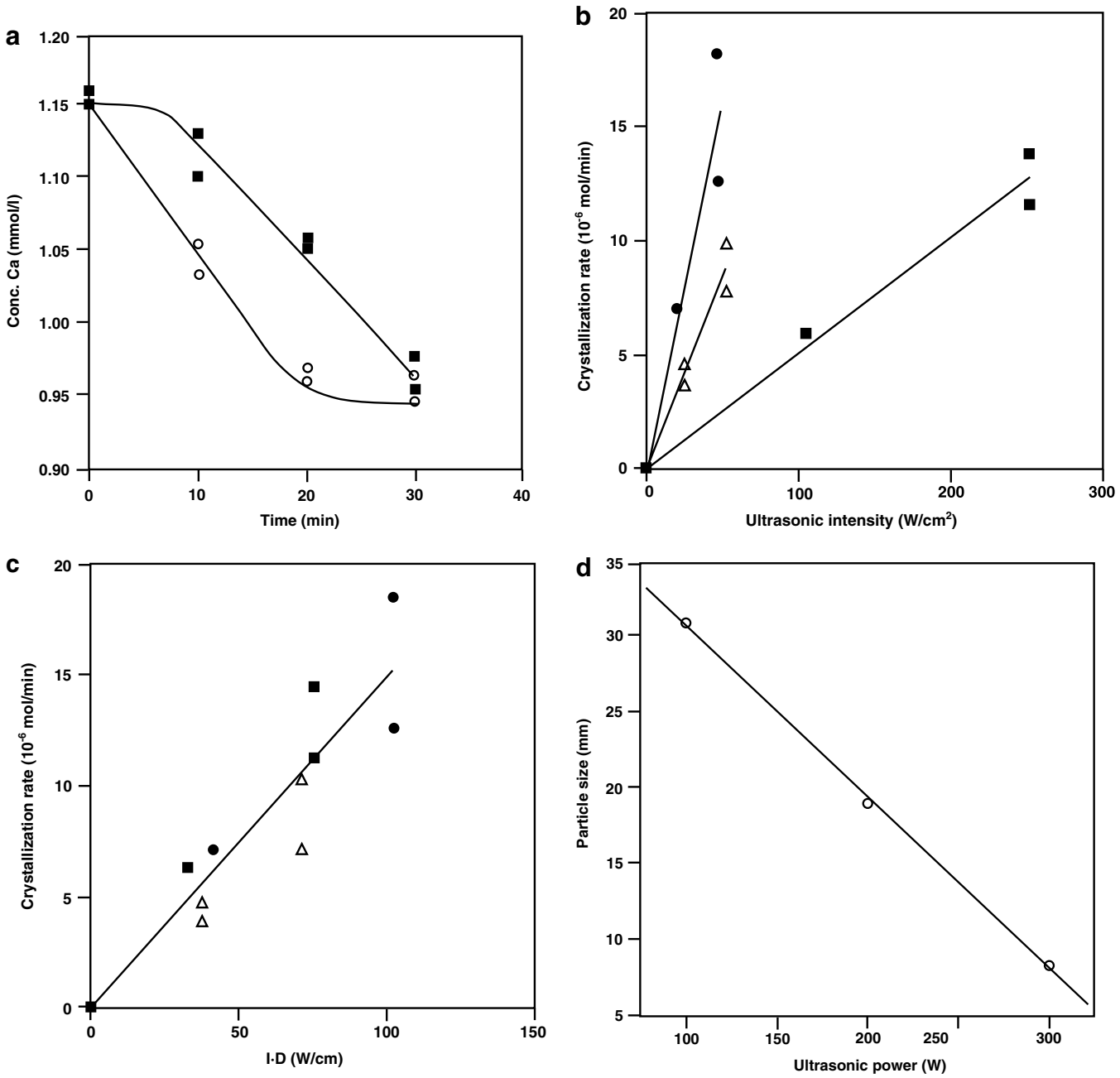

Fig. 3. (a) Influence of US intensity on calcium carbonate crystallization expressed as free [Ca^{2+}]. US intensity: (■) 250 W/cm^2, (○) 105 W/cm^2 (horn tip diameter and immersion depth 3 mm and 3 cm, respectively). (b) Variation of the crystallization rate of calcium carbonate with the US intensity at variable horn tip diameters: (■) 3 mm, (△) 14 mm, (●) 22 mm (horn immersion depth 3 cm). (c) Variation of the crystallization rate of calcium carbonate with the product of the US intensity and square root of the horn tip area. Horn tip diameter and immersion depth as in B. (d) Variation of the particle size of hydroxyapatite as a function of the US power (Reproduced with permission of Elsevier, Refs. [7,9]).

waves, so vibration and cavitation at some point in the liquid are lower. This results in fewer nuclei, and hence in larger crystals being formed. Also, increased liquid volumes provide larger free spaces for crystals to reduce collision and abrasion with each other [12].

4.5. Effect of US duration

Increasing the US irradiation time gives rise to the following sequence: at short times, the US wave fails to blend the solution and precipitant uniformly, so little precipitate is obtained after insonation; longer times produce apparent crystals the size of which decreases under continuous sonication [8].

These results demonstrated that it is possible to "tailor" a crystal size distribution between the extreme cases of a short burst of US to nucleate at lower levels of supersaturation and allow growth to large crystal, and the production of small crystal *via* continuous (or perhaps a longer single burst) US application throughout the duration of

the process, which can facilitate prolific nucleation at higher levels of supersaturation at the expense of some crystal growth. Pulsed or intermittent application of US can give intermediate effects. In any event, the optimum needs to be determined by experimental investigation. Particle size control has been demonstrated for a number of molecules including sorbitol hexaacetate, where more regularly shaped crystals can be formed [13].

4.6. Effect of ultrasound on crystal characteristics and growth

Whether US irradiation affects the characteristics of the crystals formed seemingly depends on the particular system. Thus, some authors have obtained similar crystals in the presence and absence of US [5,7], whereas others have reported substantial differences [14,15]. In the antisolvent crystallization of roxithromycin in an acetone–water mixture, the crystals exhibit a hexagonal and rhombus shape in the absence and presence of US, respectively [6]. This has been ascribed to an increased or decreased growth rate of some crystal faces under the influence of hot spots, which can alter the crystal lattice; on the other hand, abrasion may have some effect on the crystal habit.

In the case of small molecules and with high (labile) levels of supersaturation, high nucleation rates, along with concomitant poorly controlled crystallization, led to the proliferation of a distinct needle habit, manifesting itself in poorly stirred slurries and variable product bulk density. Conversely, when a solution was treated with US at much lower levels of supersaturation, a highly desired rhombic-plate-type habit was easily produced. In addition to controlling the habit, careful sonication regimes allowed the particle size to be controlled [16].

Judicious application of US to a polymorphic system at the right level of supersaturation can assist in isolating the ground-state polymorph (the most thermodynamically favoured and less soluble) or one near the ground state. This availability to induce the formation of a given polymorph under US action is of paramount importance in the pharmaceutical industry.

In crystallization processes induced by the addition of an antisolvent, where high supersaturation levels may be produced very rapidly, it has been shown that the application of US reduces not only the induction times of nucleation but also the spread of variability in induction time at a given level of supersaturation [17,18]. Typically, in antisolvent-based crystallizations the antisolvent is added to the point of precipitation, which can lead to high supersaturation levels. For a number of molecules it has been shown that significantly less antisolvent can be used in conjunction with US to induce crystallization in a controlled manner.

Sonocrystallization also avoids the problems involved in intentional seeding, very common in industrial crystallization process. The effects of intentional seeding include narrowing of the MZW, shortening of induction times, and control of particle size distribution. In a batch process, seeds have to be added at precisely the correct time during the development of the supersaturation profile. Addition too soon to a solution that is under-saturated will results in the seeds dissolving. Seeding too late will also be ineffective because the solute material may already have rapidly (and possibly disastrously) crystallized as a result of high supersaturation levels with ensuing high nucleation rates, giving a product of inferior physical characteristics. Extremely small seed crystals generated by sonication offer all the advantages of conventional seeding without many of the drawbacks such as handling, actual physical size of the seeds, when to add to a batch process, and higher quality of the seed. The exact point of nucleation, in terms of nucleation, can be well controlled, and to a degree the number of nuclei generated as a result of the prevailing supersaturation level.

The effects of US on crystal growth do not appear to be as dramatic as those on nucleation and arise largely from enhanced bulk-phase mass transfer. The mechanical disturbances created by both cavitation and ultrasonic streaming alter the fluid dynamics and increase bulk-phase mass transfer of solute to the surface of the growing crystal. The surface nucleation and integration effects at the crystal surface determine, however, the growth rate of each individual face and, hence, the habit of the crystal.

Theoretical studies suggest that the effects of US on crystal growth rate depend on the magnitude of the supersaturation driven force [19]. At low supersaturation, with growth velocities at the crystal faces around 10^{-10} m/s, the application of US doubles the growth rate, while at higher supersaturation with growth velocity around 10^{-7} m/s there appeared to be no effect. The Burton–Cabrera–Frank theory of crystal growth without sonication postulated that growth rate is limited by the formation of new surface layers at defect sites and predicts that the growth rate will exhibit approximately quadratic dependence on supersaturation at low supersaturation levels, while at higher levels the dependence becomes closer to linear [20]. The US effect is explained by the hypothesis that, at low supersaturation, the quantity of available growth units in the vicinity of the crystal surface is small. Under these conditions, bulk-phase mass transfer becomes rate limiting in supplying growth units to the crystal surface, and its ultrasonic enhancement will enhance the growth rate.

It has recently been demonstrated that the optical absorption in ionic crystals induced by X-rays and γ-irradiation can be remarkably removed by ultrasonic treatment of the crystals at room temperature. This new method of a cold annealing of radiation defects in solids can be used for particle detectors to decrease or cure a radiation damage of crystals scintillators [21].

5. Scale-up and -down sonocrystallization

One of the most important barriers to the adoption of power ultrasound technology in manufacturing has been

the lack of suitable equipment for use in industrial environments at the scale required. Most discoveries in US application have been carried out in laboratories on the milligram-to-gram scale using either high-intensity probe or bath devices.

There is a fundamental requirement of equipment that may be operated simply and reliably at the kilogram-to-ton scale in the small-volume manufacturing of fine chemicals and pharmaceuticals and importantly in an explosion-proof environment. For bulk-commodity chemicals manufacturing, scales of at least an order of magnitude larger than this would be required. Although the cost-benefit basis of the technology makes it less attractive for this type of application, all processes should be examined on a case-by-case basis, as evidenced by in bulk alumina production [22].

There are also potential applications for power US technology that are sealed down from the conventional laboratory to the microgram-to-milligram scale [23]. These consist mainly of applications to microscale mixing, and to work close to the discovery phase of pharmaceutical development where only very small quantities of material will be available. Recent publications in this field illustrate the utility of US-assisted crystallization and how relatively simple probe systems can be used to improve crystallization processes and become new tools for the process chemist [24,25].

Concerning the equipment needed for working at scales other than common laboratory scale, the design challenge for scaled-up units is to arrange multiple transducers to give a reasonably uniform intensity distribution throughout a realistic working volume. Probe systems operating at typical face intensities of 10^4–10^6 W/m^2 at frequencies of 20–60 kHz suffer the disadvantage that the intense cavitation field cannot be transmitted for more than a few cm beyond the end of the probe. Even banks of probes have been found incapable of transmitting cavitation through distances of 100–700 mm. To achieve high-intensity fields in large volumes, it is preferable to operate at a lower face intensity ($\approx$100 W/m^2) over an extended area and place multiple transducers around the medium being sonicated [26,27].

Scaled-down processes can be developed either using common baths or probes and reducing the volume of the vessel or the tip size, respectively, according to the size of the system under study.

6. Trends in sonocrystallization

The present trend from users to apply US to initiate and control crystallization processes will attract more attention than sonochemistry in the near future as US allows a new dimension of control over the nucleation regime, and may allow the nucleation-crystal growth balance to be regulated in order to optimize the product and particle properties.

New equipment development will be focused mainly on the design of large cells fitted with multiple transducers for larger-scale processes.

The evidenced potential of US to produce micrometer-sized particles for drug inhalation [28–30], as well as to nucleate nanophases, either amorphous or partially ordered, will be massively used.

Biotechnological aspects, such as the isolation and crystallization of proteins, will also benefit by US.

In developing areas of nanotechnology could also exploit the high potential of US and it is foreseeable the appearance of new applications areas after developing and improving general understanding of the relationship between US, nucleation and crystal growth.

Acknowledgements

The Spanish Ministerio de Educación y Ciencia is gratefully acknowledged for financial support (project No. CTQ 2006-01614). F. Priego Capote is also grateful to the Ministerio de Ciencia y Tecnología for an FPU scholarship.

References

[1] J.W. Mullin, Crystallization, fourth ed., Butterworth–Heinemann, Woburn, MA, 2001.
[2] Nucleation Control, Royal Society Discussion Meeting, London, (2002).
[3] D. Kashchiev, D. Verdoes, A.G. Van Vermolen, J. Cryst. Growth 110 (1991) 373.
[4] N. Lyczko, F. Espitalier, O. Louisnard, J. Schwartzentruber, Chem. Eng. J. 86 (2002) 233.
[5] E. Dalas, J. Cryst. Growth 125 (1992) 27.
[6] Z. Guo, M. Zhang, H. Li, J. Wang, E. Kougoulos, J. Cryst. Growth 273 (2005) 555.
[7] I. Nishida, Ultrason. Sonochem. 11 (2004) 423.
[8] H. Li, J. Wang, Y. Bao, Z. Guo, M. Zhang, J. Cryst. Growth 247 (2003) 192.
[9] T. Ishitsubo, E. Matsubara, S. Kai, M. Hirao, Acta Mater. 52 (2004) 423.
[10] C. Li-yun, Z. Chuan-bo, H. Jian-feng, Mat. Lett. 59 (2005) 1905.
[11] H. Li, J. Cryst. Growth 247 (2003) 192.
[12] N. Amara, B. Ratsimba, A.M. Wilhelm, H. Delmas, Ultrason. Sonochem. 8 (2001) 265.
[13] H.W. Anderson, J.B. Carbery, H.F. Staunton, B.C. Sutradhar, US Patent 5 471 001, 1995.
[14] N. Enomoto, M. Katsumoto, Z. Nakagawa, J. Ceram. Soc. Jpn. 102 (1994) 1105.
[15] N. Enomoto, J. Akagi, Z. Nakagawa, Ultrason. Sonochem. 3 (1996) S97.
[16] G. Ruecroft, D. Hipkiss, T. Ly, N. Maxted, P.W. Cains, Org. Process Res. Dev. 9 (2005) 923.
[17] L.J. McCausland, P.W. Cains, Chem. Ind. 5 (2002) 15.
[18] L.J. McLausland, P.W. Cains, P.D. Martin, Chem. Eng. Prog. 9 (2001) 56.
[19] V.S. Arakelyan, Acta Phys. Hung. 61 (1987) 185.
[20] W.K. Burton, N. Cabrera, F. Frank, Phylos. Trans. A 243 (1951) 299.
[21] I. Ostrovskii, IEEE Trans. Nucl. Sci. 52 (2005) 3068.
[22] G. Ruecroft, D. Hipkiss, M. Fennel, TMS 2005, TMS Light Metals 2005.
[23] L.J. McCausland, P.W. Cains, M. Maxwell, Chem. Ing. Tech. 73 (2001) 717.
[24] R.D. Dennehy, Org. Process Res. Dev. 7 (2003) 1002.

[25] S. Kim, C. Wei, S. Kiang, Org. Process Res. Dev. 7 (2003) 997.
[26] P.D. Martin, W.L. Ward, Trans. IChemE 70A (1992) 296.
[27] C.L. Desborough, et al., Brit. Patent Appl. GB 2 243 092 A.; C.L. Desborough, et al., Eur. Patent Appl. EP 0 449 008 A (1991).
[28] R.W. Lancaster, H. Singh, A.L. Theophilus, World Patents WO 02 00199 A1, 2002; WO 02 00200 A1, 2002, WO 01 38811, 2000.
[29] P. Rogueda, World Patent WO 05 004847 A1, 2005.
[30] R. Price, J.S. Kaerger, World Patent WO 05 073827, 2005.