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Effect of ultrasonic irradiation on morphology and polymorphic transformation of glycine

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ABSTRACT

The polymorphic phase transformation of β-glycine to α-glycine was analyzed in the absence and presence of three different intensities of ultrasonic irradiation in a batch system at 25 °C. The experiments were performed to explore the effects of ultrasonic irradiation and its intensity on phase transformation time, morphology, storage stability, and filtration characteristics. The crystals obtained with and without ultrasound were characterized by X-ray diffraction (XRD). The XRD results showed that the ultrasound tended to reduce the transformation time. According to the scanning electron microscopy (SEM) images, the ultrasound had a significant effect on the crystal morphology. The highest ultrasound power applied yielded more rounded crystals compared to the crystals prepared in the absence of ultrasound. In addition to SEM analysis, detailed crystal shape analysis was performed and shape factors, namely the circularity, elongation, and convexity values, were determined quantitatively to get more information about the morphological changes related to the variations in the size and shape of the end products. From the morphological point of view, the circularity values of the crystals obtained under ultrasound were higher but the elongation values were smaller compared to the crystals obtained in the absence of ultrasound. It was also found that higher ultrasound decreased the length and width of the crystals, and the application of ultrasound increased the aspect ratio value from 0.483 to 0.657.

1. Introduction

Glycine is the simplest amino acid and has widespread use in the chemical, cosmetics, pharmaceutical, and food industries. Its three polymorphs under atmospheric temperature and pressure are the γ, α, and β forms, which are the most stable polymorph of glycine, the metastable polymorph of glycine, and the unstable polymorph of glycine, respectively [1–5]. α-Glycine at room temperature is stable and spontaneously crystallizes from aqueous solution. Both β and γ nucleation are usually obtained only under certain conditions, such as in the presence of alcohol and additives, or with technical processes at extreme temperatures [6,7]. Polymorphs generally have different chemical and physical properties, including stability, crystal shape, compressibility, melting point, thermal conductivity, heat capacity, density, and dissolution rate [8]. These differences in chemical and physical properties result in the need to handle and process the materials differently [9]. Thus, the control of polymorphism is of great importance for efficient crystal production [10]. Ultrasound is used to improve the quality of the end-products and control polymorphism. Use of ultrasound in crystallization processes is reported to alter the crystal habit and crystal size distribution, help or hinder agglomeration, and facilitate product handling [9]. Some studies have indicated that different polymorphs can be formed with different physical properties when systems are treated with ultrasound. Nii and Takayanagi [11] performed a study to investigate the impact of high-frequency ultrasound on the crystallization behavior of the polymorphs of glycine in a water–ethanol system. The transformation between β and α forms was carried out in non-sonicated and sonicated media. Ultrasonic transducers operating at 1.6 MHz and 20 kHz were used and the influence of ultrasonic frequency was investigated by comparing the resulting crystals produced by these two ultrasound frequency. They found that the crystal size was reduced at low frequency ultrasound; however, ultrasound enhanced both the growth rate of α-glycine crystals and the incorporation of microcrystals into larger crystals. Renuka et al. [12] studied to determine the higher ultrasonic frequency effects on the nucleation and growth characteristics of glycine. The experiments were performed at different ultrasound frequencies in the range of 1–10 MHz. They found that higher ultrasound yielded a higher nucleation rate but with a smaller crystal size compared to the crystals obtained in the absence of ultrasound. A similar study performed by Louhi-Kultanen et al. [13] showed that ultrasound affected the crystal morphology and crystal size distribution of glycine. These studies were

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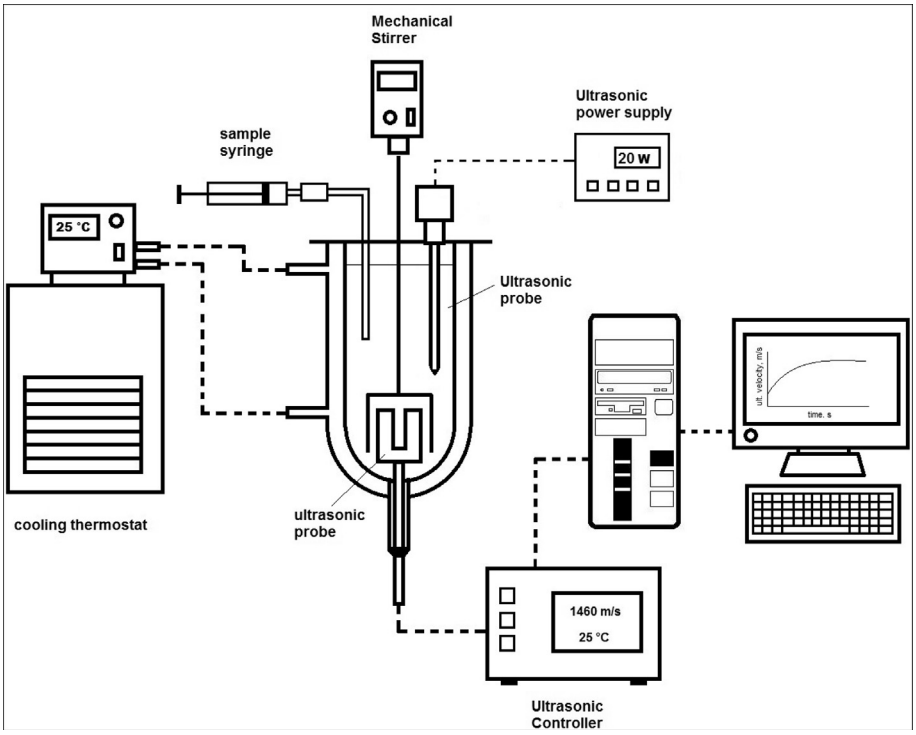

Fig. 1. Experimental setup.

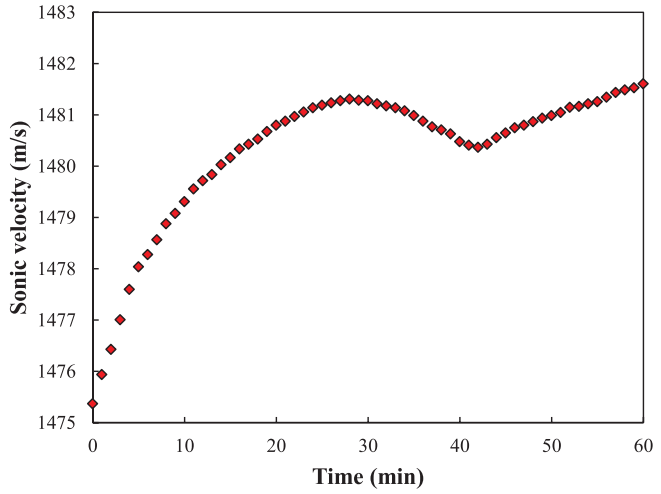

Fig. 2. The variation of ultrasonic velocity versus time during the transformation process in the absence of ultrasound.

performed to investigate the influence of ultrasonic irradiation on the particle size and distribution. However, the crystal shape factors, such as circularity, elongation, and convexity, have not been studied and there is a lack of studies focusing on particle shape which has similar importance degree. Therefore, the effects of ultrasonic irradiation on the morphology and crystal shape of glycine were investigated. The measurement of particle shape in addition to size is important in order to improve the operation conditions efficiently and reproducibly [14]. The operation conditions, such as flowing, mixing, wetting, and drying of solids, are dependent on the characteristics of the solids. In order to produce a quality product with the desirable properties, such as flowability and filterability, particle shape factors should be known. Detailed identification of crystal shape with interpretation and representation of shape parameters would provide useful information for various industries where glycine is used. Furthermore, as an important physical property of polymorphic crystals, the stability of the crystals was examined to improve the quality of the as-obtained glycine crystals and to obtain detailed information on the effects of ultrasonic irradiation on the glycine polymorphs formed. To date, no previously reported study has focused on the storage stability of glycine polymorphs precipitated using a liquid antisolvent method in the presence of ultrasonic irradiation. A better understanding of the stability of crystals is of great importance to increase the productivity of the glycine transformation process. Therefore, the purpose of this study was threefold: to determine the influence of ultrasonic irradiation on the morphology and storage stability of glycine, to describe the particle shape parameters quantifiably, and finally, to detect the impact of sonication on the time taken for the phase transformation from the β to the α form of glycine.

2. Experimental methods

Crystallization experiments were carried out in a 2-litre double-jacketed glass crystallizer in the absence and the presence of an ultrasonic source. Pure powdered α-glycine (Merck), ethanol (Merck), and triple distilled water were used in all experiments. A schematic representation of experimental setup is given in Fig. 1. The inner temperature of the crystallizer was kept constant at 25 ± 0.1 °C by means of circulating water from the thermostated bath into the crystallizer jacket. Stirring was performed with a specially designed paddle-type Teflon stirrer. The stirring rate was set to 75 rpm and kept constant. A Bandelin ultrasound homogenizer Sonopuls HD 2200 equipped with a 3 mm diameter immersion probe was used as the ultrasonic source, working at 20 kHz frequency and 200 W maximum power. The experiments were conducted at three different ultrasonic powers of 20, 30, and 40 W.

Firstly, the transformation of β-glycine to α-glycine was carried out in the absence of ultrasonic irradiation. At the beginning of the experiment, according to solubility data at 25 °C, the appropriate amount of α-glycine was dissolved in 500 ml of triple distilled water and filtered using a membrane filter with a nominal pore size of 0.45 μm. The saturated and filtered solution of α-glycine at 25 °C was placed in the crystallizer, stirred well at 75 rpm, and kept at 25 °C in media without the application of ultrasonic irradiation. After reaching thermal

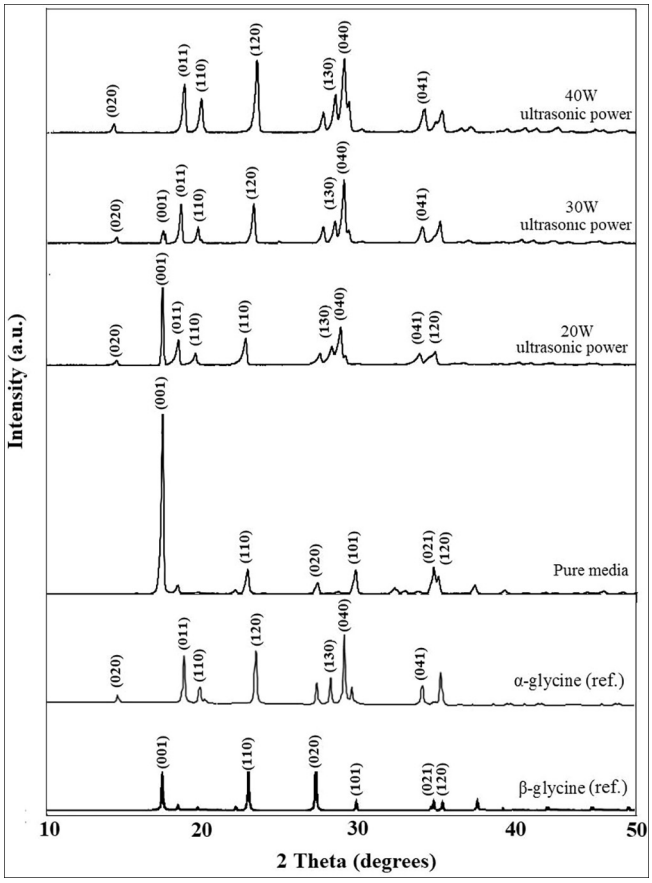

Fig. 3. XRD results of the crystals obtained in the absence and presence of ultrasound at t = 8 min.

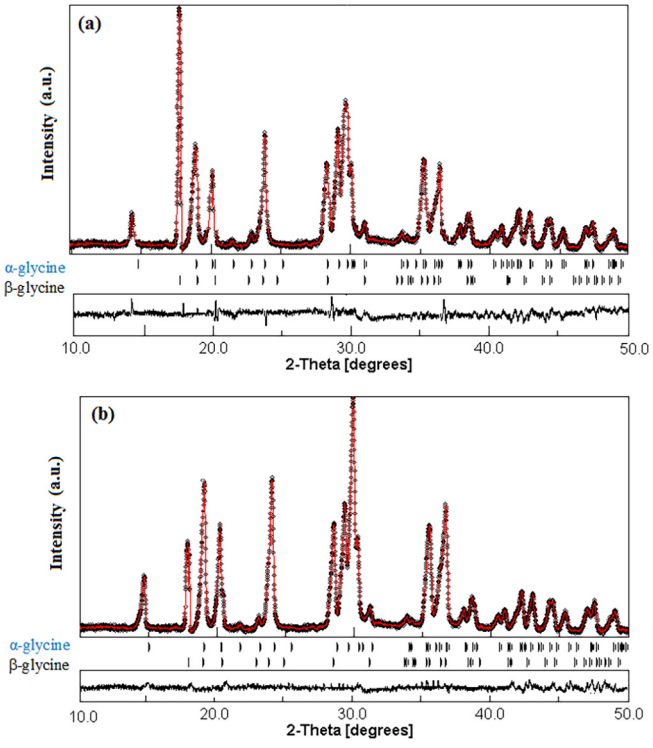

Fig. 4. Structural Rietveld refinement for the glycine crystals obtained in the presence of 20 W (a), and 30 W (b) ultrasonic power at t = 8 min.

equilibrium, polymorph β was produced from anti-solvent crystallization. The volume fraction of ethanol used as anti-solvent in the suspension was 0.67. When the anti-solvent was rapidly mixed with the saturated solution, the β form appeared instantly and then slowly transformed into the α form. In pure media, namely media without an ultrasonic source, this polymorph transformation during the crystallization was followed by measuring the ultrasonic velocity of the suspension. Ultrasonic velocity measurement was carried out with an ultrasonic sensor (LiquiSonic 30, SensoTech GmbH) with an accuracy of ± 0.01 m/s. This sensor emits longitudinal ultrasonic waves with very low frequency and these waves do not have a cavitation effect in the suspension.

To determine the influence of ultrasonic irradiation on the polymorph transformation, an ultrasonic probe was directly immersed into the suspension and ultrasound was applied at the top of the crystallizer with a titanium tip. During the transformation process, both without and with ultrasonic irradiation, the samples were withdrawn from the crystallizer at regular time intervals, quickly filtered, and then the solid phase was dried and analyzed. Scanning electron microscopy (SEM) was used to observe the morphology of the crystals obtained whilst X-ray diffraction (XRD) analysis was used to determine the crystal structure and demonstrate the phase transition. SEM images of the crystals were taken using a Zeiss EVO LS 10 scanning electron microscope. XRD analysis of the crystals was carried out using a Bruker D2 Phaser Table-top Diffractometer with Cu Kα radiation at 30 kV at a rate of 0.01°/s in the range of 10–50°. Quantitative phase analysis of the samples was accomplished using the Rietveld refinement method employing the Materials Analysis Using Diffraction (MAUD) software developed by Wenk, Matthies & Lutterotti and Ferrari & Lutterotti. Differential scanning calorimetry (DSC) was also used to determine the polymorphic forms of the crystals. 5 ± 0.5 mg of the sample was taken in an aluminum pan and heated over the temperature range between 30 and 400 °C at a heating rate of 10 °C/min under a constant N_2 flow rate. To get a better insight into the size and shape characteristics of the crystals obtained with and without ultrasonic irradiation, the crystals were characterized using a Malvern Morphologi G3 instrument. This instrument allows analysis of the shape and size parameters by means of scanning and recording the images of all measured crystals. The 10× lens was utilized for all the analysis. In addition to these analyses, filtration tests were carried out at 700 mbar in the standard filtration system for the crystals produced in the absence and presence of ultrasound. Once the transformation process was complete, 250 ml of suspension extracted from the crystallizer was transferred to the filtration unit, and then collection time for each 10 ml of filtrate under constant pressure was measured and recorded. At the end of the process, total filtrate volume and filter cake height were measured. The obtained results were evaluated according to Darcy's law, whereby glycine filtration characteristics like average specific cake resistance and average cake porosity were calculated.

3. Results and discussion

3.1. Ultrasonic velocity measurement

The ultrasonic velocity through liquid media is a physical property that depends on the density and adiabatic compressibility of the media, which changes with temperature, concentration and pressure. Changing the ultrasonic velocity of a solution has been successfully used to measure the in situ changes in concentration of a solute. The polymorphic phase transition can be monitored using the change in the ultrasonic velocity; the change in the concentration and thereby the change in the ultrasonic velocity can be observed during the polymorphic phase transition due to the dependence of the ultrasonic velocity on the concentration [15]. Therefore, the polymorph transformation process of β-glycine to α-glycine in pure media was monitored through online measurement of the ultrasonic velocity in this study.

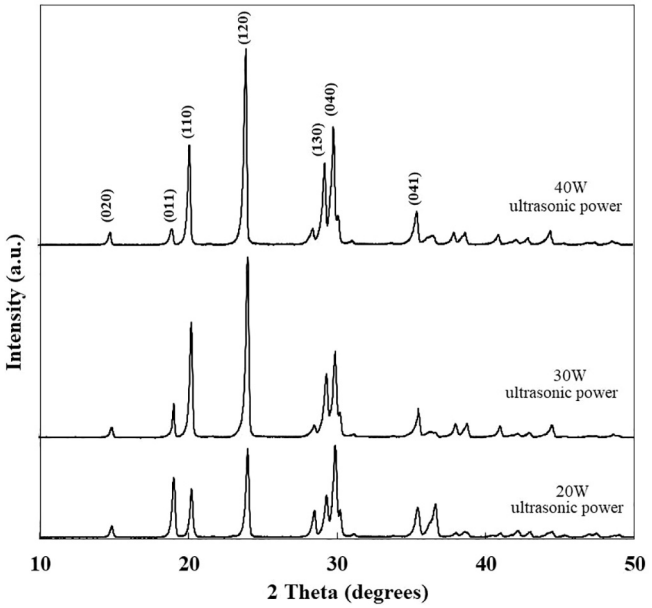

Fig. 5. XRD results of the end products obtained under different ultrasonic irradiation.

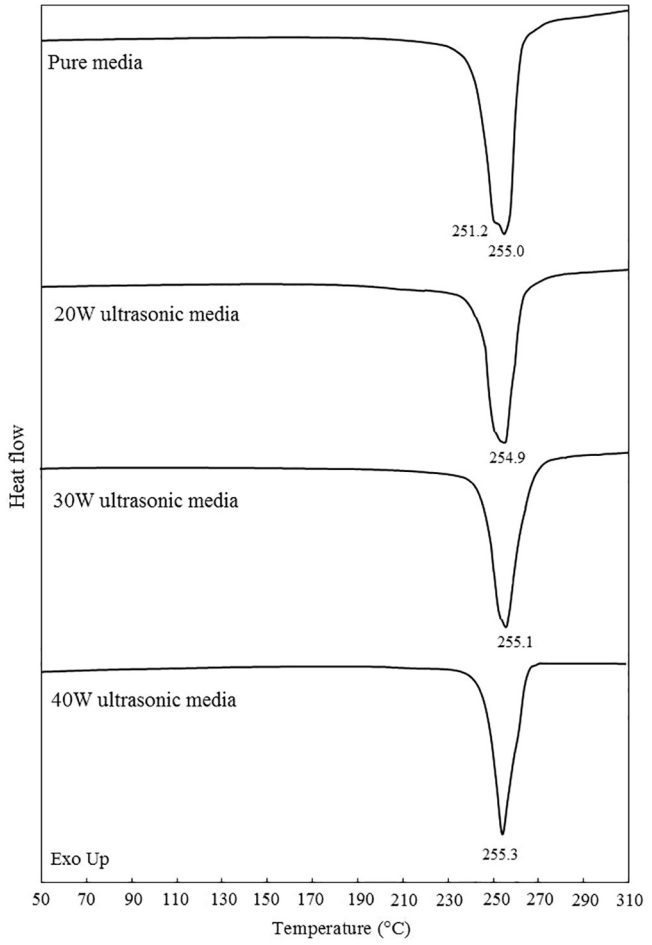

Fig. 6. DSC results of the crystals obtained in the absence and presence of ultrasonic irradiation.

The graph of the changes of the ultrasonic velocity in the absence of ultrasonic irradiation over time is shown in Fig. 2. According to Fig. 2, the transformation process took place in three stages. These were, consecutively, dissolution of β-glycine crystals, formation of the α-glycine nuclei, and the growth of α-glycine crystals. In the first stage, ultrasonic velocity increased with the dissolution of β-glycine crystals. Then, a sharp change and a significant decrease were observed at 42 min. At this point, formation of α-glycine nuclei, having a more stable thermodynamic composition, was observed. After this point, ultrasonic velocity increased again with the growth of α-glycine crystals.

3.2. XRD and DSC

The transformation process of the crystals produced in the presence of an ultrasonic source was monitored through XRD analysis of the samples taken at certain time intervals. XRD results of crystals obtained at t = 8 min in the absence of an ultrasonic source and in the presence of three different intensities of ultrasonic irradiation are shown in Fig. 3. The XRD results clearly revealed that the polymorph transformation time depended on the ultrasonic intensity applied. Increasing the intensity of ultrasonic irradiation shortened the transformation time. At t = 8 min, the crystals obtained in the absence of ultrasonic irradiation had a specific peak at 2θ = 18° showing the β form of glycine and the other peaks detected were also linked to β-glycine [16]. At low ultrasonic irradiation, while this specific peak was dominant, new peaks appeared at 20° and 29°, which were characteristic of α-glycine [5]. At 30 W ultrasonic irradiation, the intensities of these peaks changed. The characteristic β-glycine peak intensity decreased, whereas the intensities of α-glycine peaks increased. The Rietveld refinements applied for the crystals produced under an ultrasonic power of 20 W or 30 W at t = 8 min are given in Fig. 4. This analysis method demonstrates the close fit of the peaks observed in the experimental patterns (i.e., the observed X-ray powder diffraction pattern of the sample) with their respective simulated patterns. The method reveals that the mass fraction of β-glycine was 49.71% after ultrasonic irradiation at 20 W, which decreased upon increasing the ultrasonic power to 30 W (mass fraction of β-glycine = 11.34%). The results indicate that the formation of α-glycine was more favorable under a higher ultrasonic irradiation power. At 40 W ultrasonic power, the peaks related to the β form disappeared; i.e., the glycine crystals obtained were completely in the α form. These results showed that there was a relationship between transformation time and ultrasonic irradiation. While the phase transformation completed at t = 45 min for pure media, completion times of 25, 16, and 8 min were obtained for the crystals obtained at 20, 30, and 40 W ultrasonic power, respectively. It was noted that the transformation rate increased and the transformation time reduced with the increase of ultrasonic power applied.

XRD results of the end product obtained after the completion of the transformation process are shown in Fig. 5. The results revealed that all the crystals obtained under sonication were in the α form and that their peak intensities were changed due to the ultrasonic effect. Peak intensity was augmented in parallel to the increase in the ultrasonic power. For example, the relative intensity of the peak at 20° was around 6000 at 20 W ultrasonic power, and about 16,000 and 20,000 for the 30 W and 40 W power, respectively.

The thermal characterization of α-glycine crystals obtained by completing the polymorphic phase transformation process with and without ultrasonic irradiation was performed by DSC analyzer and the results are given in Fig. 6. The DSC curve for the crystals obtained in pure media presented two peaks among which the first peak at around 250 °C belonged to the presence of trace amount of β polymorph in the crystal. The next peak at 255 °C was attributed to the melting point of the α-polymorph [17]. On the other hand, the crystals produced in the presence of the 20, 30 and 40 W ultrasonic power had only a peak at 254.9, 255.1 and 255.3 °C, respectively. These results showed that the crystals obtained did not include any amount of the β-form and all crystals were in α form.

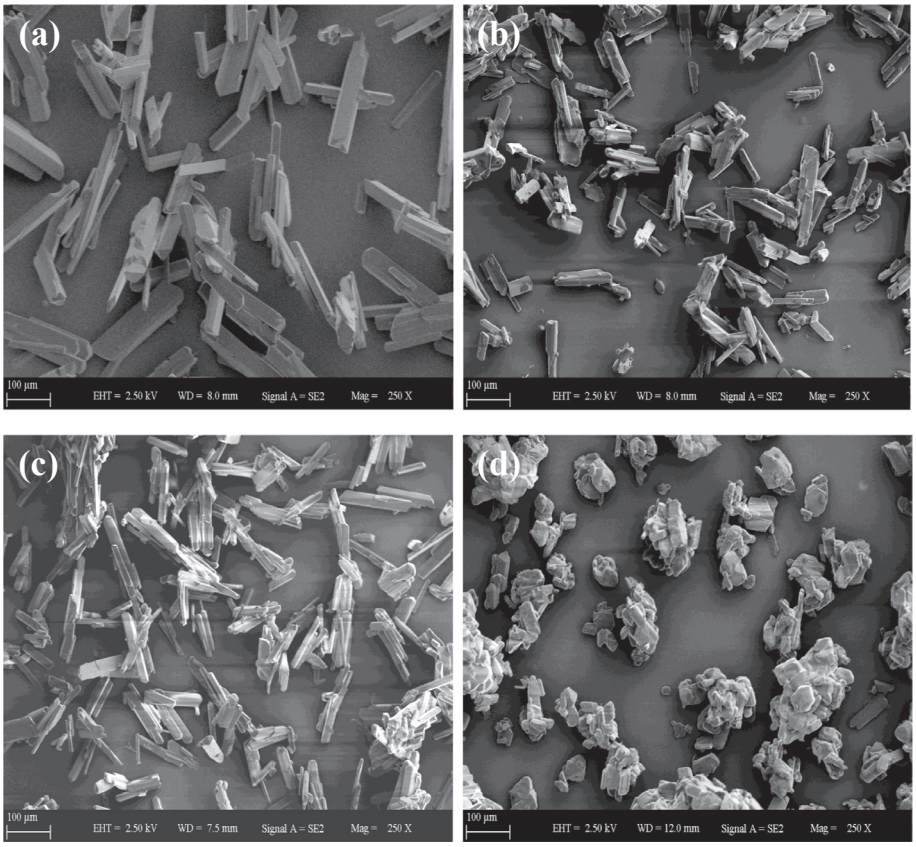

Fig. 7. SEM images of the glycine crystals in the absence (a) and presence of 20 W (b), 30 W (c), and 40 W (d) ultrasonic power.

3.3. SEM

The SEM images of α-glycine crystals obtained by completing the polymorphic phase transformation process with and without ultrasonic irradiation are given in Fig. 7. The crystals obtained in the absence of ultrasound were prismatic with a regular form and rod shape, which was consistent with previous studies [11,18]. These crystals were robust and did not undergo any breakage owing to the hydrodynamic conditions of the media. In the presence of low intensity ultrasound at 20 W, the α-glycine crystals showed successive growth behavior. Moreover, slight breakages were observed on the crystal surface due to the ultrasonic irradiation. The prismatic sharp ends of crystals tended to

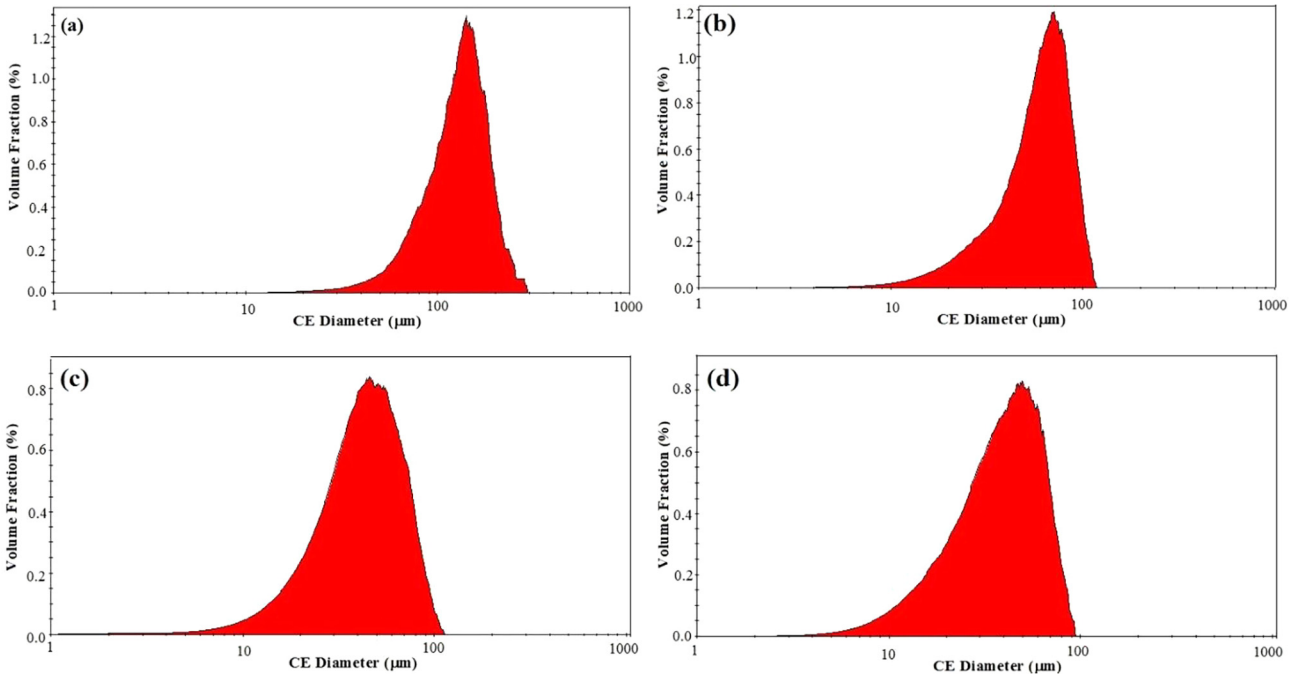

Fig. 8. The particle size distribution of the glycine crystals obtained in the absence (a) and presence of 20 W (b), 30 W, (c) and 40 W (d) ultrasonic power.

become round but they preserved their rod form. Furthermore, the particle size of the crystals was smaller compared to those prepared in the absence of ultrasonic irradiation. The crystals obtained with moderate ultrasound power of 30 W began to lose their apparent form. Deformations occurred on all crystal edges and surfaces and the amount of breakage increased significantly. Similar to the crystals obtained with 20 W ultrasonic power, the successive crystal growth behavior continued and the widths and lengths of the crystals reduced significantly. Moreover, glycine crystals obtained using 30 W ultrasonic power continued to undergo breakage. However, these effects scaled up with increasing ultrasonic intensity, with a higher effect yielded by the 30 W compared to the 20 W case. In the presence of the 40 W ultrasonic power, the crystal morphology changed entirely. The rod form was replaced by a shorter, partially rounded form, which can be attributed to the ultrasonic effect. In addition, the intensity of the ultrasonic irradiation applied caused deformations on the sharp edges of the crystals. The highest deformation, breakage, and morphological changes occurred under the 40 W ultrasonic power, and these crystals also showed intensive agglomeration. That is increase in ultrasonic power increased agglomeration.

3.4. Morphology

The morphological characteristic, that is the size and shape, of the α-glycine crystals obtained by the completion of the transformation of β-glycine into α-glycine in non-sonicated and sonicated media were examined simultaneously in detail using a Morphologi G3 device from Malvern. In this context, the particle size distributions of glycine crystals obtained under the studied conditions as well as the shape factors, like circularity, elongation, and convexity values, were determined.

Circularity is the ratio of the perimeter of a circle with the same area as the particle divided by the perimeter to the actual particle image. Circularity values range from 0 to 1. The circularity of a perfect circle is 1, while the circularity of a 'spiky' or irregular object is closer to 0. Both overall form and surface roughness can affect circularity. Therefore, the circularity approaches 1 as the shape becomes more round and smooth. The edge roughness of a particle is described by its convexity, which is calculated by dividing the convex hull perimeter by the actual particle perimeter. The convexity of a smooth shape is 1, while the convexity of a very 'spiky' or irregular object is closer to 0. Elongation is [1 − width/length] and, as implied by its name, it is a measure of elongation; its values range from 0 to 1. The elongation value of a shape that is symmetrical in all axes, e.g. a circle or a square, is 0; elongation values of shapes with large aspect ratios are closer to 1 [19–21].

Fig. 8 shows the plots of particle size distribution determined by considering the circle equivalent (CE) diameter, the diameter of a circle with the same area as the particle, of α-glycine crystals obtained by the completion of the phase transformation in the absence and presence of ultrasound. Particle size distribution curves showed normal distributions in all operating conditions, and bimodal distribution was not observed. Table 1 shows D(v, 0.1), D(v, 0.5), and D(v, 0.9) values obtained by using such particle size distributions. D(n, 0.5) is the size in micrometers at which 50% of the sample is smaller and 50% is larger, whereas D(n, 0.1) and D(n, 0.9) are the particle sizes below which 10% and 90% of the sample is distributed, respectively. The v in the expression shows that this refers to the volume distribution [16]. As can be clearly seen from Table 1, while the mean CE value was 131.6 μm in those prepared in the absence of ultrasonic irradiation, these values were measured as 60.93, 42.55, and 39.22 μm with increasing ultrasonic intensity. Accordingly, the mean projected area values decreased with increasing ultrasonic intensity. In the evaluation of approximately 40,000 crystals in the Morphologi G3 device, the length and width of the crystals were determined for non-sonicated and sonicated media. The results obtained are presented in Fig. 9a and b, respectively. As can be seen in Fig. 9, the length and width distributions of the crystals obtained in those prepared in the absence of ultrasonic irradiation were wide compared to the crystals obtained in ultrasonic media. The application of ultrasonic irradiation in crystallization media resulted in narrow distributions. Both the length and the width of the crystal distributions were narrower with increasing ultrasonic intensity. In other words, the ultrasound power was inversely proportional to the size distributions. The images of some of the crystals obtained using the Morphologi G3 are given in Fig. 10. Glycine crystals obtained in those prepared in the absence of ultrasonic irradiation have smooth surface and rod shape. With the increase of applied ultrasonic intensity, the crystals lost their smooth surface and the crystals obtained were rough. Twinning was formed in the structures and irregularities increased accordingly. Sharp edges begun to round, and breaking and abrasions increased. The highest impact was observed at 40 W, where the highest ultrasonic intensity was applied. The morphology of the crystals obtained in the media where 40 W ultrasonic intensity was applied was completely changed compared to the crystals prepared without ultrasonic irradiation. The crystals completely lost their rod form and their edges gained a different appearance by rounding. When images obtained from the Morphologi G3 device, which analyzes morphologic structures systematically, and SEM analysis performed using lower amounts of sample are compared, similar morphological changes are observed. In other words, the Morphologi G3 and SEM results were in agreement with each other. Both analytical methods clearly showed that the crystals underwent morphological change with increasing ultrasonic intensity. Shape factors such as circularity, convexity, and

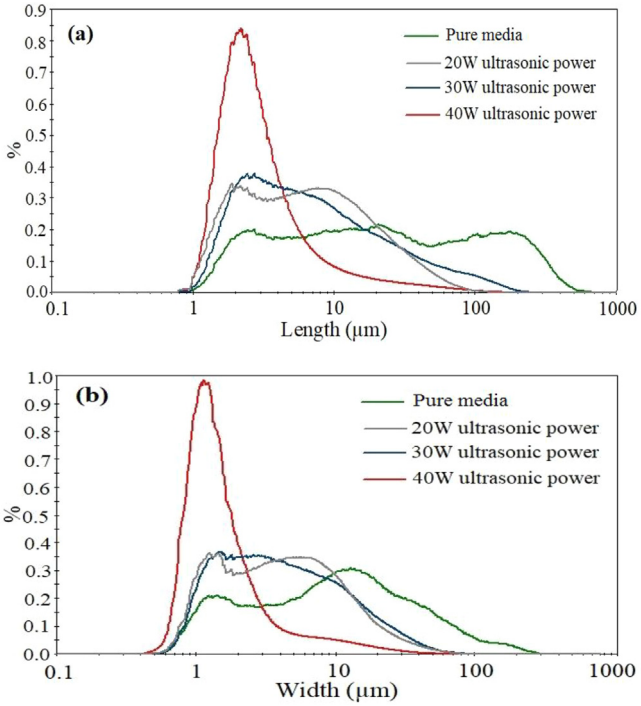

Fig. 9. The crystal length (a) and width (b) distributions obtained in the absence and presence of ultrasonic irradiation.

Table 1
Values of CE diameter according to volume distribution and mean area.

Media	CE diameter (μm)			Mean area $(\mu m)^2$
	D (0.1)	D (0.5)	D (0.9)	
Without ultrasound	74.01	131.6	179.4	1939.18
20 W ultrasonic power	27.95	60.93	84.64	205.92
30 W ultrasonic power	19.63	42.55	70.93	103.37
40 W ultrasonic power	16.35	39.22	64.55	27.16

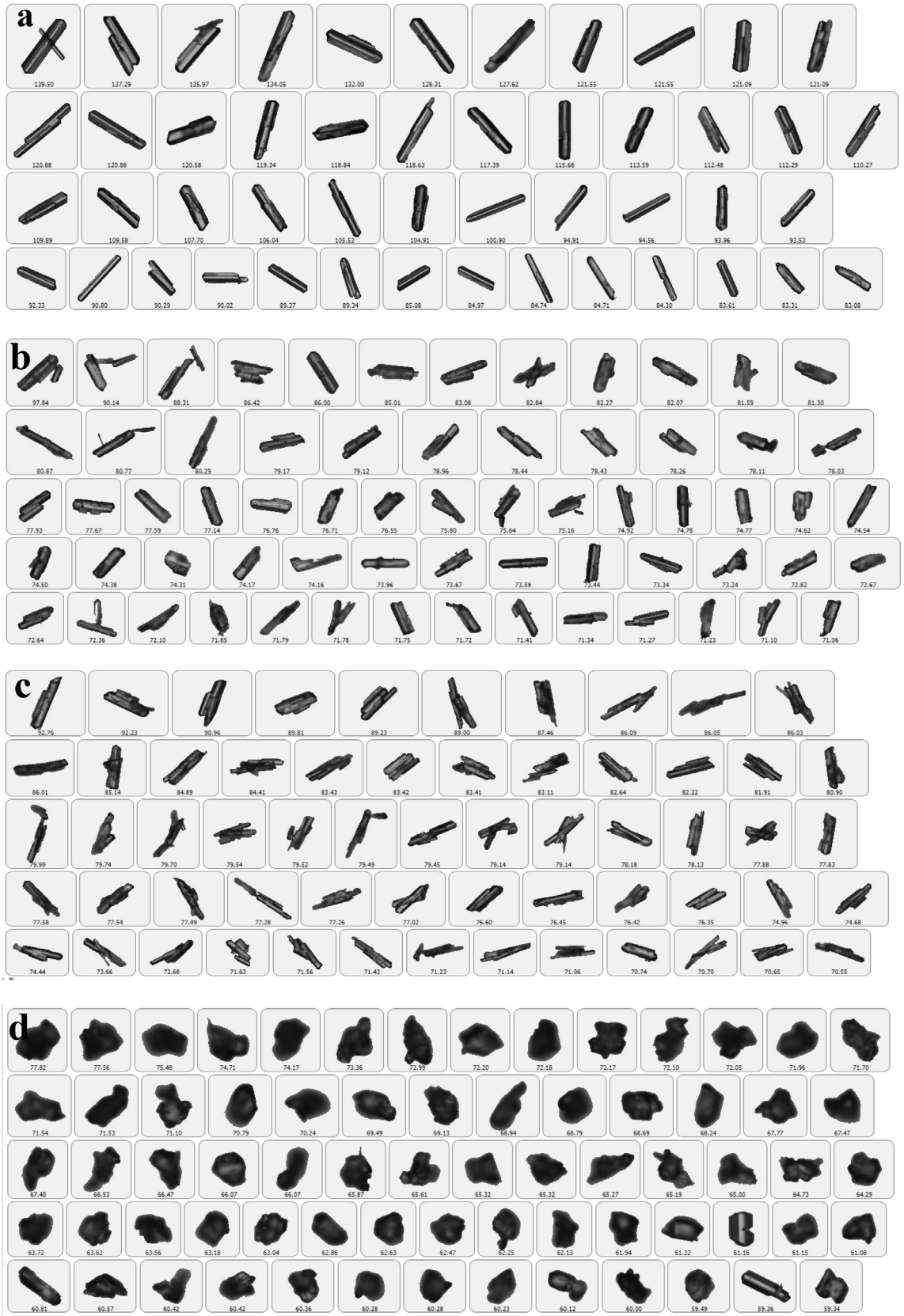

Fig. 10. The shapes of the crystals obtained in the absence (a) and the presence of 20 W (b), 30 W (c), and 40 W (d) ultrasonic power.

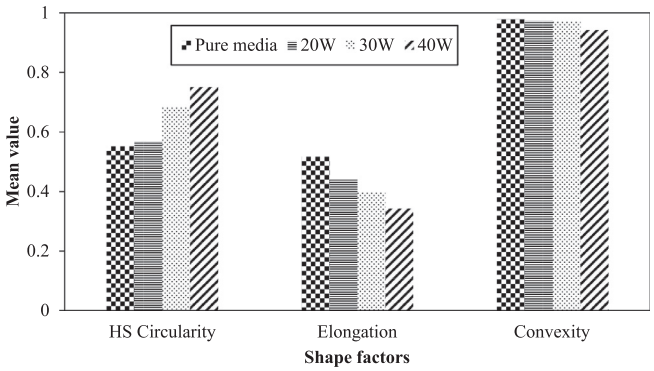

Fig. 11. Variation of the crystal shape factor values of the crystals obtained in the absence and presence of ultrasound.

elongation were examined to quantify the measured shape of the crystals. Fig. 11 shows the variation of the calculated particle shape factor values of the crystals obtained in the absence and different ultrasonic media. As can be clearly seen from Fig. 11 while the high sensitivity (HS) circularity value of the glycine crystals obtained by the completion of the phase transformation process in the absence of ultrasonic irradiation was 0.552, this value reached a maximum value of 0.751 with increasing ultrasonic intensity. It is expected that the circularity value is low because the crystals obtained without ultrasonic irradiation media have a rod-like structure. At the same time, the elongation value determined by considering the shapes of the crystals seems to have a higher value than the crystals produced in the ultrasonic media. The fact that the elongation value calculated for the crystals obtained without ultrasonication higher than the elongation value of the crystals produced in the ultrasonic media supports this result. As the ultrasonic impact increases, the circularity value increases while the elongation value decreases. On the other hand, it was determined that the convexity value, which characterizes the shape factor, was between 0.979 and 0.942, and it was independent from the ultrasonic impact. Aspect ratios obtained by dividing the width of the crystal by its length were calculated in order to determine the aggregation tendency in the working conditions. The aspect ratio value determined as 0.483 in the absence of ultrasonic irradiation increases to 0.657 with the ultrasonic power at 40 W. This is an indication that agglomeration of the crystals increases in terms of shape analysis. As a matter of fact, the images obtained from SEM and Morphologi G3 analysis support this view. Another parameter that can be used to characterize the morphology of the obtained crystals is solidity. Solidity is defined as the object area divided into areas enclosed by the convex hull area. Mean solidity value calculated for glycine crystals obtained in the absence of ultrasonic irradiation is determined as 0.910, while this value reaches to 1 with the increasing impact of ultrasonic intensity. At the same time, it is known that solidity values of morphologically very smooth rounded shapes are 1. The solidity results showed that the glycine crystals have more rounded surfaces with ultrasonic impact.

3.5. Storage stability

In this study, stability, an important physical property of polymorphic crystals, was investigated under different storage conditions. For this purpose, the stability of the glycine crystals obtained in pure media and in the presence of the 30 W ultrasonic power was studied in the dry state and in the solution state for one month. The obtained crystals were analyzed by XRD and Morphologi G3 analyzer. Fig. 12 shows the XRD analysis results for the end products obtained with and without ultrasound after 1 month of storage. As can be clearly seen from the XRD results, in all conditions that were examined, glycine remained in the α form and there was no second phase formation. The images of some of the crystals obtained using the Morphologi G3 for

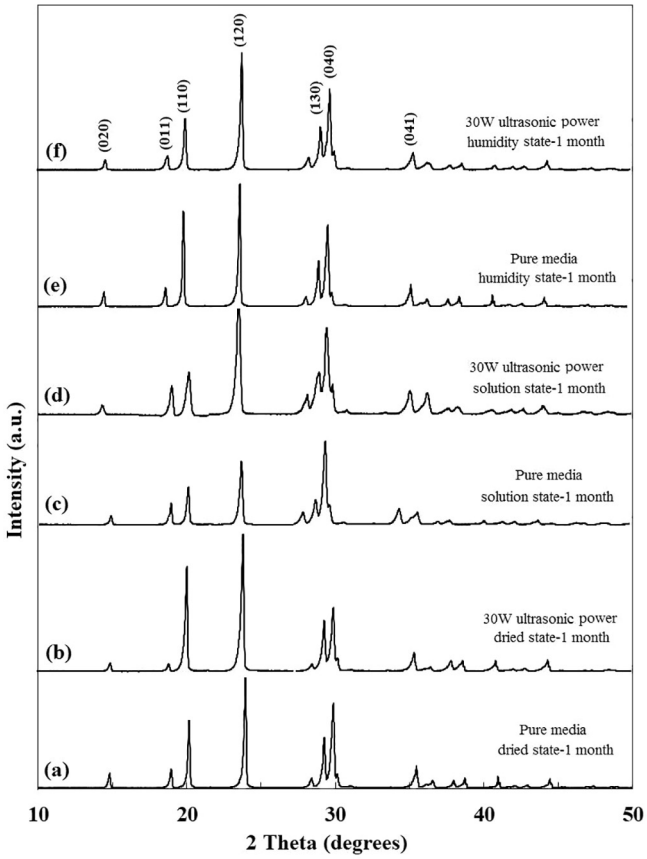

Fig. 12. XRD results for the crystals obtained in the absence and presence of 30 W ultrasonic power under different storage conditions.

dried state test conditions are given in Fig. 13. When the images of the crystals obtained in the absence of ultrasonic irradiation and stored for 1 day in the dried state were examined, the crystals had a smooth surface and were in a rod-like form. When the crystals stored for 1 month in the dried state were compared with the crystals stored for 1 day, it was seen that the crystals obtained were partially deformed and their smooth surfaces disappeared. At the same time, the aspect ratio of the crystals stored for 1 month was increased with respect to that for the crystals stored for 1 day, increasing from 0.485 to 0.529. The images of the crystals obtained with 30 W ultrasonic power and stored for 1 day and 1 month in the dried state are given in Fig. 13c and d, respectively. When the images were examined, no significant change in crystal morphology could be seen. Similarly, the aspect ratios of the crystals obtained after 1 day and 1 month storage were determined as 0.657 and 0.654, respectively. In addition, as can be seen from Fig. 14, the average particle size of the crystals obtained in the presence of 30 W ultrasonic power did not change. The 1-month stability studies carried out in the dried state conditions showed that the stability of the crystals obtained with ultrasonic irradiation was higher than that of the crystals obtained in pure media.

A similar stability study was also conducted in the solution state. The images of the crystals obtained using the Morphologi G3 are given in Fig. 15. Similar to the dried state storage results, the crystals obtained in the pure media and stored in solution were slightly deformed at the end of 1 month of storage whereas no morphological change was observed for the crystals obtained in the ultrasonic media. The aspect ratios of the crystals obtained in pure media and in the presence of ultrasound after 1 day of storage were 0.489 and 0.657, respectively, and 0.541 and 0.652 after 1 month of storage, respectively. This clearly indicates that the ultrasonic effect enhanced the stability of the glycine crystals. Moreover, the storage stability of α-glycine crystals was

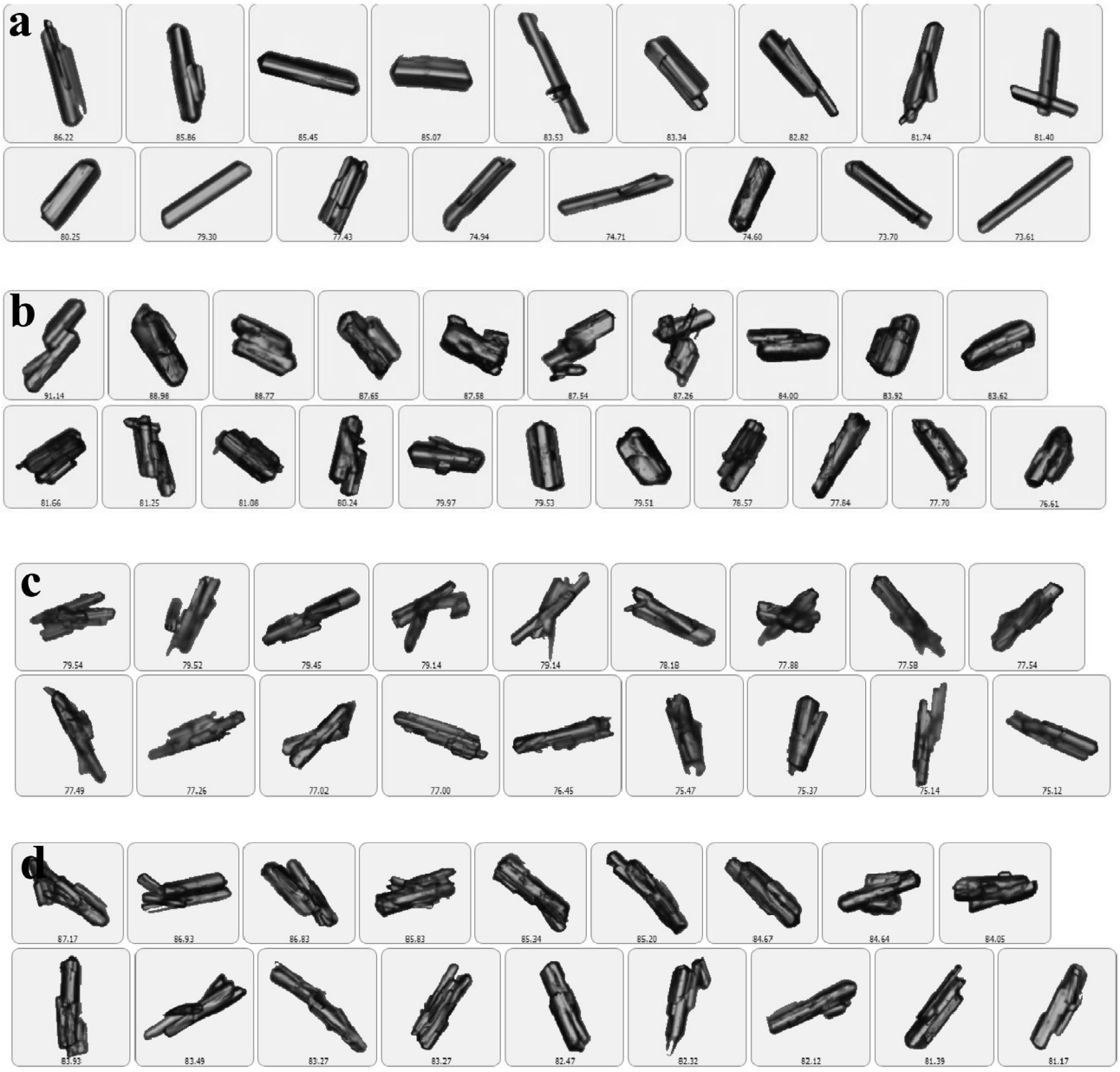

Fig. 13. The shapes of the crystals obtained in (a) pure media and stored for 1 day, (b) pure media and stored for 1 month, (c) 30 W ultrasonic power and stored for 1 day, and (d) 30 W ultrasonic power and stored for 1 month under dried state conditions.

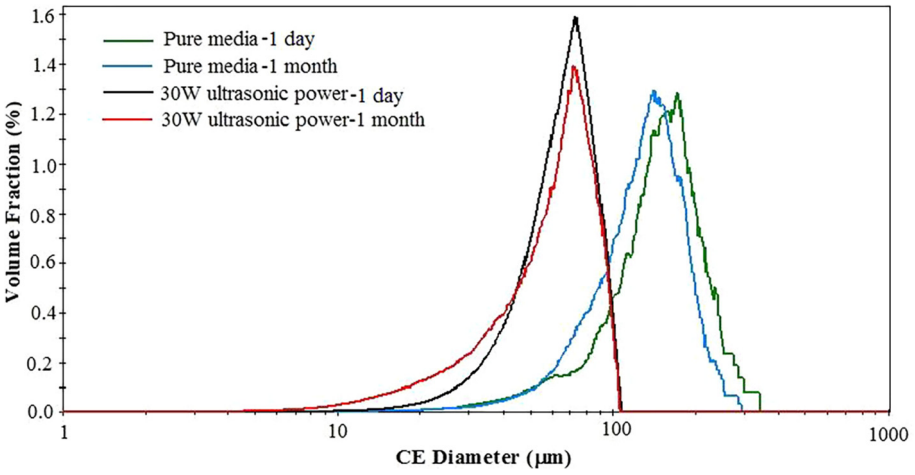

Fig. 14. The particle size distribution of the glycine crystals obtained in the absence and presence of 30 W ultrasonic power under dried state conditions.

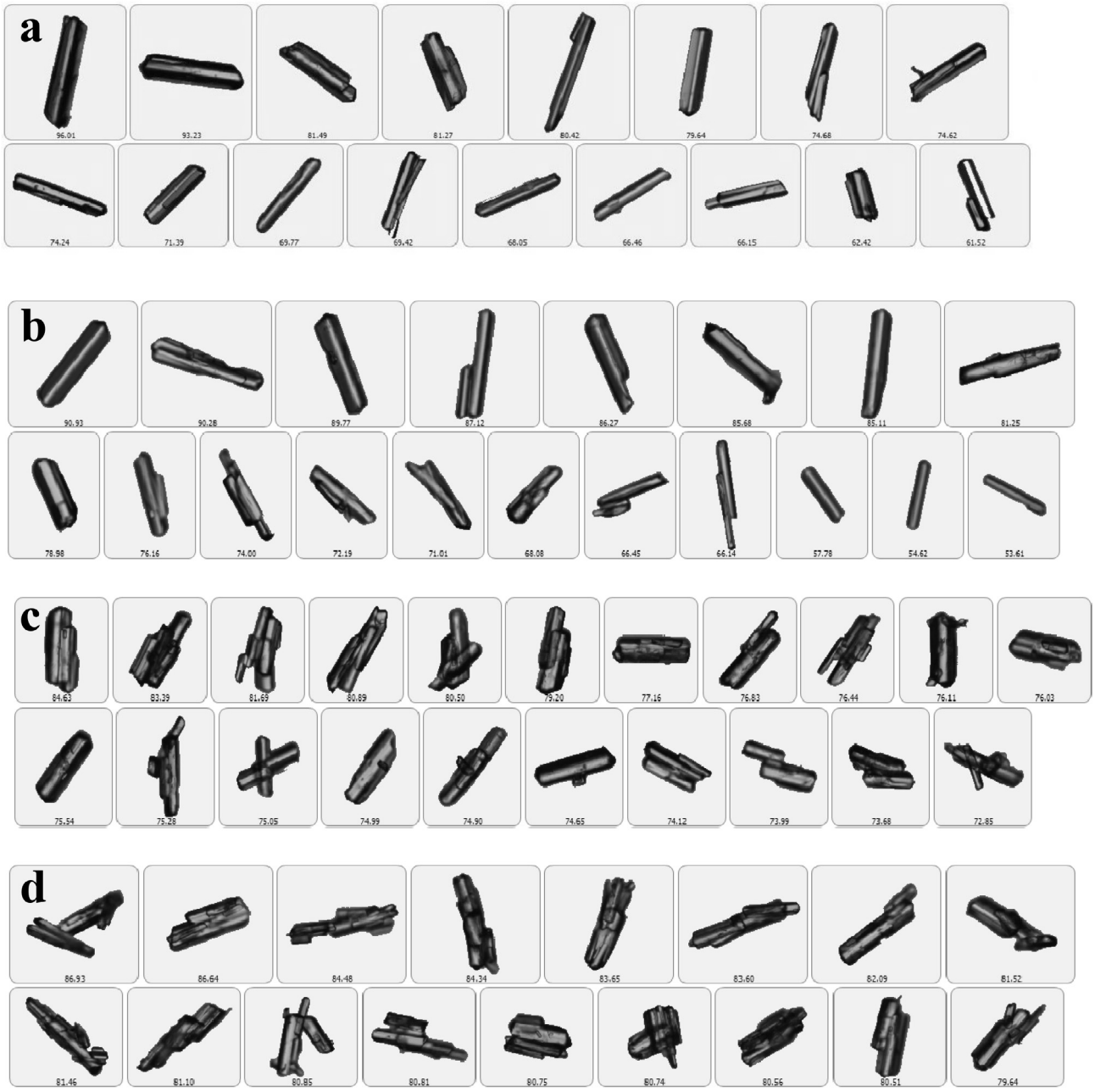

Fig. 15. The shapes of the crystals obtained in (a) pure media and stored for 1 day, (b) pure media and stored for 1 month, (c) 30 W ultrasonic power and stored for 1 day, and (d) 30 W ultrasonic power and stored for 1 month under solution state conditions.

investigated under humid condition (40 °C, 75% RH). The images of the crystals are given in Fig. 16. There was no significant change in the morphology and average particle size of the crystals obtained both without and with ultrasonic irradiation.

3.6. Filtration characteristics

To investigate the influence of ultrasonic irradiation and its intensity on the filtration characteristics of the glycine crystals, the filtration rates of the crystals obtained under both pure and sonication conditions were measured; the dry cake mass and cake height were also determined. The average specific cake resistance and the average filter cake porosity were calculated using these data according to Darcy's law [22]. The specific cake resistance of the glycine produced without ultrasonic irradiation was calculated as 1.095×10^{11} m/kg. Under 20 W ultrasonic power, the filtration rate of the crystals decreased and the specific cake resistance was determined to be 2.146×10^{11} m/kg. Such an increase in the specific cake resistance may suggest morphological changes of crystals as well as breakage induced by the ultrasonic irradiation. Owing to the extended breakage in presence of 30 W ultrasonic power, the specific cake resistance increased similarly to the crystals obtained at 20 W ultrasonic power, and was calculated to be 3.055×10^{11} m/kg. However, this increasing tendency in specific cake resistance was not observed at 40 W ultrasonic power. The specific cake resistance of α-glycine crystals obtained at this power was determined as 8.023×10^{10} m/kg. Compared to both media without ultrasonication and the various ultrasonic powers studied, the observed decrease can be attributed to the change of the crystal habit. As shown in the SEM image of the crystals obtained at 40 W ultrasonic power, unlike the crystals obtained with 20 W and 30 W ultrasonic power, the crystals

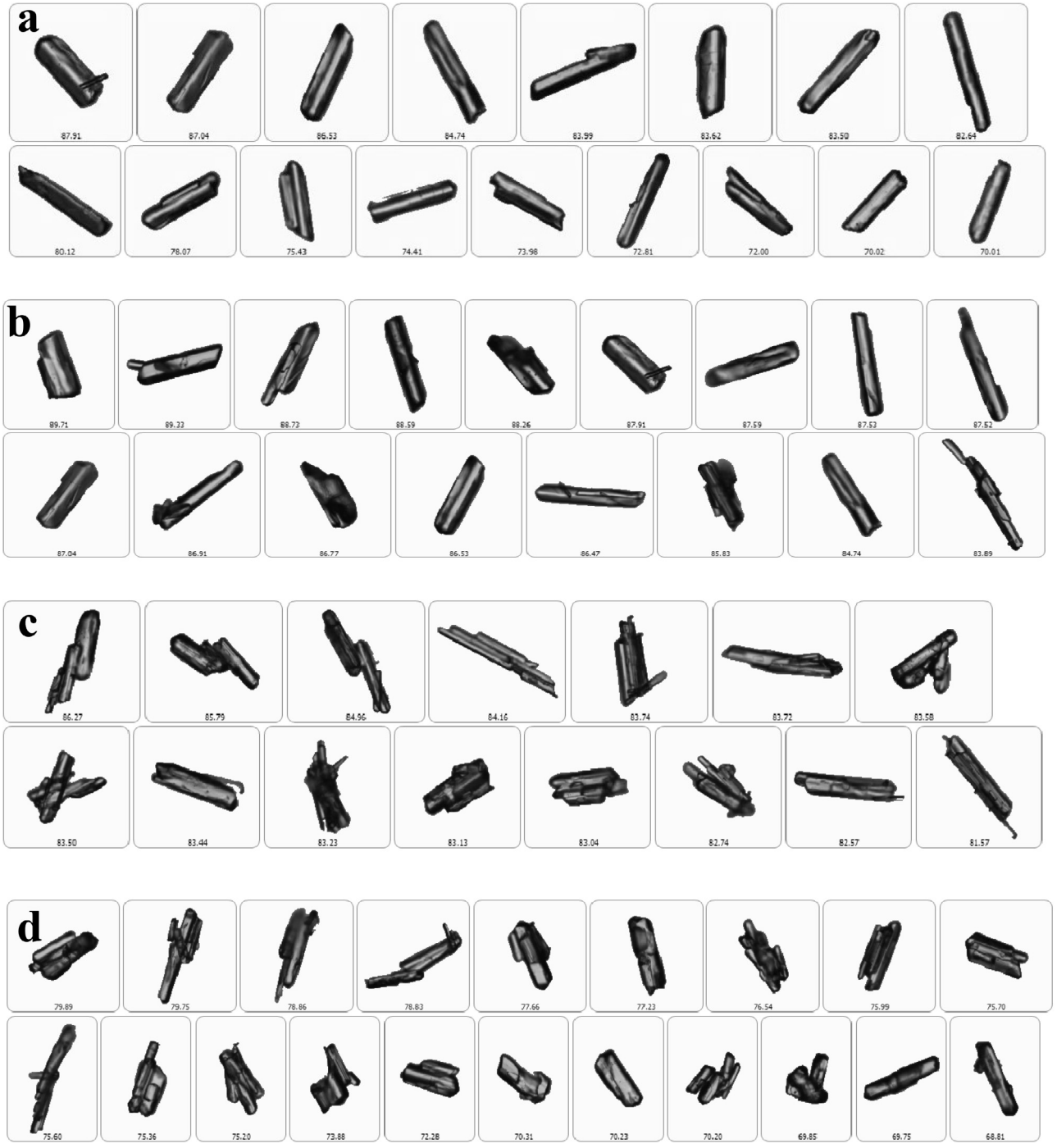

Fig. 16. The shapes of the crystals obtained in (a) pure media and stored for 1 day, (b) pure media and stored for 1 month, (c) 30 W ultrasonic power and stored for 1 day, and (d) 30 W ultrasonic power and stored for 1 month under humid conditions.

formed compact and stable aggregates. This type of aggregate directly affected the filtration characteristics of the crystals. The cake porosities of the crystals were identified in addition to the average specific cake resistance. The cake porosity was calculated according to the results of the filtration rate measurements conducted at 700 mbar. For the glycine crystals obtained in the absence of ultrasonic irradiation, this was calculated to be 0.421. The cake porosity decreased with increasing ultrasonic power. The average cake porosities were determined as 0.441 and 0.319 for the crystals obtained in the presence of 20 and 30 W ultrasonic power. On the other hand, an approximately 5% increase was observed in the cake porosity in the presence of 40 W ultrasonic power compared to the media without sonication due to the morphologic differences of the crystals.

4. Conclusions

The scope of this study was to investigate the impact of ultrasonic irradiation on the phase transformation process of glycine from the β to the α form. The phase transformation time was shortened with increasing ultrasonic irradiation. SEM analysis showed that the morphology of the glycine crystals was affected by ultrasonic irradiation and fairly large differences were observed in the shapes and sizes of the

crystals obtained with different power. Glycine crystals obtained in media without the application of ultrasonic irradiation were prismatic and rod forms, but the crystals were transformed into the shorter partially rounded form in the presence of ultrasound. Moreover, deformation, breakage, and agglomeration occurred under ultrasonic irradiation. The results of morphology analysis showed that the mean projected area, width, and length of the crystals decreased with increasing ultrasound power. The circularity value also increased while the elongation value decreased as the ultrasonic power increased. The changes in particle shape parameters and morphology characteristics seen in the presence of ultrasonic irradiation directly affected the filtration characteristics of glycine crystals. While the specific cake resistance of the glycine obtained in the absence of ultrasonic irradiation was calculated as 1.095×10^{11} m/kg, these values varied from 8.023×10^{10} to 3.055×10^{11} m/kg for crystals produced under ultrasonic irradiation.

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References

[1] Y. Iitaka, The crystal structure of β-glycine, Acta Crystallogr. B 13 (1960) 35–45.
[2] P.G. Jonsson, A. Kvick, Precision neutron diffraction structure determination of protein and nucleic acid components. III. The crystal and molecular structure of the amino acid α-glycine, Acta Crystallogr. B 28 (1972) 1827–1833.
[3] K. Srinivasan, Crystal growth of α and γ glycine polymorphs and their polymorphic phase transformations, J. Cryst. Growth 311 (2008) 156–162.
[4] M. Shishido, K. Amasaka, Solution crystallization of glycine by using microcapillary system, Kagaku Kougaku Ronbunshu. 30 (2004) 177–179 (in Japanese).
[5] M. Matsumoto, Y. Wada, A. Oonaka, K. Onoe, Polymorph control of glycine by antisolvent crystallization using nitrogen minute-bubbles, J. Cryst. Growth 373 (2013) 73–77.
[6] K.R. Devi, V. Gnanakamatchi, K. Srinivasan, Attainment of unstable β nucleation of glycine through novel swift cooling crystallization process, J. Cryst. Growth 400 (2014) 34–42.
[7] K.R. Devi, K. Srinivasan, Synthesis, bulk growth, polarizability and nonlinear optical properties of γ-glycine single crystals, Cryst. Res. Technol. 50 (2015) 389–394.
[8] T.L. Threlfall, Analysis of organic polymorphs a review, Analyst 120 (1995) 2435–2460.
[9] S. Gracin, M. Uusi-Penttila, A.C. Rasmuson, Influence of ultrasound on the nucleation of polymorphs of p-aminobenzoic acid, Cryst. Growth Des. 5 (2005) 1787–1794.
[10] R.K. Garg, D. Sarkar, Polymorphism control of p-aminobenzoic acid by isothermal anti-solvent crystallization, J. Cryst. Growth 454 (2016) 180–185.
[11] S. Nii, S. Takayanagi, Growth and size control in anti-solvent crystallization of glycine with high frequency ultrasound, Ultrason. Sonochem. 21 (2014) 1182–1186.
[12] K.R. Devi, A. Raja, K. Srinivasan, Ultrasound assisted nucleation and growth characteristics of glycine polymorphs – a combined experimental and analytical approach, Ultrason. Sonochem. 24 (2015) 107–113.
[13] M. Louhi-Kultanen, M. Karjalainen, J. Rantanen, M. Huhtanen, J. Kalla, Crystallization of glycine with ultrasound, Int. J. Pharm. 320 (2006) 23–29.
[14] J.F. Bauer, Pharmaceutical solids: size, shape, and surface area, J. Valid. Technol. 15 (2009) 37–44.
[15] J. Ulrich, L.B.M.J. Jones, Speed of sound, in: A. Chianese, H.J.M. Kramer (Eds.), Industrial Crystallization Process Monitoring and Control, Wiley-VCH Verlag GmbH, Weinheim, Germany, 2012, pp. 59–69.
[16] Z. Liu, L. Zhong, P. Ying, Z. Feng, C. Li, Crystallization of metastable β glycine from gas phase via the sublimation of α or γ form in vacuum, Biophys. Chem. 132 (2008) 18–22.
[17] T. Tari, R. Ambrus, G. Szakonyi, D. Madarasz, P. Frohberg, I. Csoka, P. Szabo-Revesz, J. Ulrich, Z. Aigner, Optimizing the crystal habit of glycine by using an additive for impinging jet crystallization, Chem. Eng. Technol. 40 (2017) 1323–1331.
[18] X. Yang, J. Lu, X.J. Wang, C.B. Ching, Effect of sodium chloride on the nucleation and polymorphic transformation of glycine, J. Cryst. Growth 310 (2008) 604–611.
[19] Morphologi G3 User Manual MAN0410 Issue3.0, April 2010. < https://www.malvern.com/en/products/product-range/morphologi-range/morphologi-g3 > .
[20] E. Olson, Particle shape factors and their use in image analysis-part 1: theory, Summer 15 (2011) 85–96.
[21] E.J. Liu, K.V. Cashman, A.C. Rust, Optimising shape analysis to quantify volcanic ash morphology, GeoRessj 8 (2015) 14–30.
[22] A. Rushton, A.S. Ward, R.G. Holdich, Solid-Liquid Filtration and Separation Technology, second ed., Wiley-VCH Verlag GmbH, Weinheim, Germany, 2000.