19th European Symposium on Comminution & Classification (XIX ESCC)
September 27–30, 2026, Naples - Italy

Laboratory-Scale Assessment of Shear and Impact Attrition of Carbamazepine Dihydrate Crystals during Agitated Filter Bed Drying

Wei Pin Goh*, Mojtaba Ghadiri

School of Chemical and Process Engineering, University of Leeds, Leeds LS2 9JT, UK

Abstract. Agitated filter bed drying (AFBD) is a key pharmaceutical operation but can induce attrition in mechanically fragile crystals. Using carbamazepine dihydrate as a model, this study combines a lab-scale AFBD surrogate with an FT4 Powder Rheometer® and an aerodynamic dispersion method to probe shear- and impact-driven breakage. Results show progressive, multi-regime attrition, initial crystal snapping followed by surface chipping, governed by impeller clearance, consolidation load, solvent content, and energy input, providing a material-efficient framework for optimising AFBD process.

1. Introduction

In the pharmaceutical industry, agitated filter bed drying (AFBD) is a critical unit operation for isolating, dewatering, and drying potent active pharmaceutical ingredients (APIs). The inclusion of mechanical agitation is essential for promoting heat and mass transfer uniformity, preventing channelling, and ensuring homogeneous drying of the filter cake. However, the application of an impeller also introduces significant mechanical stresses into the particle bed, frequently resulting in undesirable particle size reduction through shear deformation, frictional contacts, and particle–particle or particle–impeller interactions. These effects are particularly pronounced for fragile crystalline materials, where uncontrolled breakage can compromise both product quality and downstream processability.

The behaviour of a particle bed during agitated drying is governed by a complex interplay of material properties and operating conditions, which together dictate the balance between particle breakage and agglomeration. Bagster and Bridgwater [1] investigated material flow in agitated dryers and demonstrated that bed dynamics are strongly influenced by impeller geometry and operating configuration, particularly blade height, blade angle, and bed depth. These geometric parameters affect local shear fields, stress distributions, and flow regimes within the bed. Complementary studies by Lekhal *et al.* [2, 3] further highlighted the sensitivity of crystal properties to key process variables, including agitation rate, temperature, and pressure. Their work showed that particle breakage is favoured under conditions of low drying rates and/or high shear rates, whereas agglomeration tends to dominate at high drying rates and/or low shear rates. They also reported that impact-induced breakage occurs primarily at high impeller speeds, while shear-induced breakage within the bulk of the particle bed is the more prevalent and dominant attrition mechanism [4].

Despite the recognised importance of these mechanisms, experimental investigation of agitated drying remains challenging. Over the years, numerous laboratory-scale agitated dryers have been developed to study drying under controlled conditions [5–8]. However, most of these systems are in-house instruments designed within academic settings and are therefore not readily available to the pharmaceutical industry. Furthermore, laboratory setups intended to replicate industrial-scale heat and mass transfer behaviour and mechanical stress environments often require relatively large quantities of material, which are typically unavailable during early-stage process development. These systems also tend to lack operational flexibility, such as interchangeable impeller geometries or precise control over impeller motion, limiting their ability to probe the influence of individual process parameters systematically[9].

To address this limitation, a laboratory-scale agitated filter bed dryer was developed in collaboration with Freeman Technology as an auxiliary attachment for the FT4 Powder Rheometer®. This AFBD surrogate enables simulation of the agitated filter bed drying process under well-controlled conditions and allows particle attrition arising from bulk shear deformation, consolidation, and impeller-induced stresses to be directly observed and quantified. In the present work, carbamazepine dihydrate (CBZ·$2H_2O$) is selected as a model compound for systematically studying particle breakage phenomena during agitated drying. CBZ·$2H_2O$ is particularly well suited to this role due to its acicular shape, high propensity for fracture, pharmaceutical relevance, and well-documented crystal structure and mechanical anisotropy.

To complement the FT4-based AFBD, which primarily interrogates breakage under shear and

* Corresponding author: w.p.goh@leeds.ac.uk

compressive loading, a second, orthogonal breakability assessment technique was developed to specifically examine impact-driven attrition. This method employs the aerodynamic dispersion unit of the Morphologi G3 to induce high-velocity particle impacts. This approach enables systematic evaluation of particle fragmentation as a function of impact energy while requiring only minimal quantities of material.

Together, these complementary techniques demonstrate that particle breakage in carbamazepine dihydrate is a multi-regime, progressive process. This combined experimental framework provides a powerful means of disentangling the relative contributions of shear- and impact-induced damage, offering valuable insight for the rational design and optimisation of AFBD processes for mechanically fragile pharmaceutical solids.

2. Carbamazepine dihydrate

Carbamazepine dihydrate crystals incorporate two water molecules within their crystal lattice, forming continuous channels that extend along the longest dimension of the macroscopic crystal and are aligned with the crystallographic c-axis. The crystal structure is monoclinic, belonging to the space group $P2_1/c$ [10]. The crystals typically display acicular and platy morphologies, which arise from anisotropic growth behaviour: the growth rates associated with the dominant crystal faces {h00} and {0k0} are significantly higher than those along the third crystallographic direction. As a result, the b and c axes correspond to the particle length and width of the formed crystals (Figure 1).

The ordered arrangement of water channels within the lattice gives rise to weak cleavage planes of the {0k0} family, which are oriented perpendicular to the dominant {h00} face. These cleavage planes are mechanically fragile and can be readily exposed during dehydration, as stress is relieved within the lattice [11]. Cracking on the {h00} faces, aligned parallel to the c-axis, has been observed and is attributed to the removal of water molecules from the channel structure [12] (Figure 2). Material preparation have previously been prepared [13, 14].

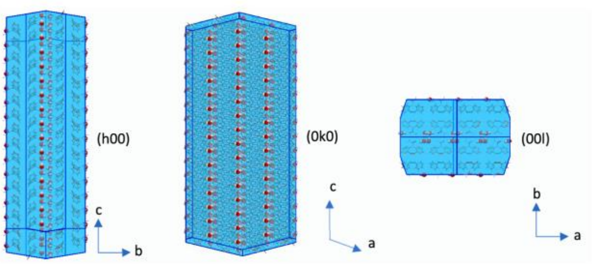

Figure 1. Calculated Bravais, Friedel, Donnay and Harker (BFDH) crystal morphology of carbamazepine dihydrate.[13]

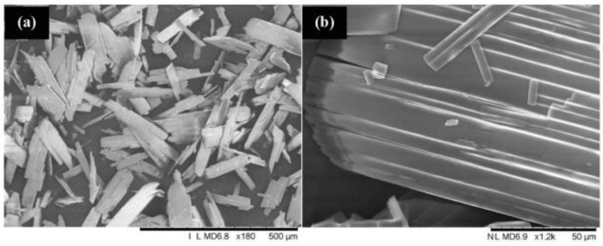

Figure 2. (a) Carbamazepine dihydrate crystals viewed by scanning electron microscope (SEM); (b) Formation of cracks on weak cleavage planes along (h00) face under vacuum in the SEM chamber due to dehydration. [13]

3. Impact Breakage Assessment by Aerodynamic Dispersion Method

In our investigation into impact-induced breakage, we utilised the aerodynamic dispersion unit of a Morphologi G3 to subject carbamazepine dihydrate to controlled mechanical stress. This method employs a pulse of pressurised air, ranging from 0.5 to 5.0 barg, to accelerate minute powder samples against the internal walls of an entrainment spool. To establish a quantitative link between process parameters and breakage, we performed transient three-dimensional Computational Fluid Dynamics (CFD) modelling to predict the normal impact velocities of the particles within the disperser. By tracking particle trajectories through a Lagrangian approach, we were able to calculate average impact velocities for various size classes, which served as critical inputs for our modified version of the Ghadiri and Zhang impact breakage model.

$$R^* = \beta\rho \sum_{i=1}^{n} \phi_i D_i U_i^2$$

where R^* is the fractional mass loss, β the breakability index, ρ the particle density, i the bin number, φ the volume fraction of the particles, D the representative particle size, and U the corresponding particle impact velocity in bin i. Our analysis revealed that the breakage of these acicular crystals is inherently non-linear and operates across two distinct mechanical regimes. In the first regime, which corresponds to lower dispersion pressures, we observed rapid fragmentation where the crystals predominantly snap along their largest dimension. This "snapping" mechanism is driven by geometric bending moments acting on the high-aspect-ratio particles and was characterised by a breakability index of 0.47. As the particles became more equant through initial breakage, we identified a transition to a second regime dominated by chipping and surface erosion, which exhibited a significantly lower breakability index of 0.20 (Figures 3 & 4).

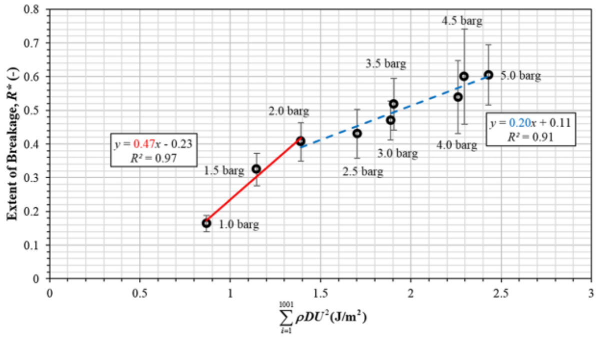

Figure 3. Extent of breakage as a function of ρDU^2. [13]

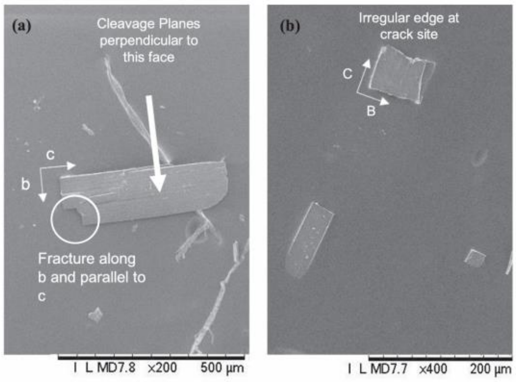

Figure 4. Snapping of carbamazepine dihydrate crystals. [13]

Furthermore, we gained significant structural insights into the interplay between external geometry and internal crystallographic planes of weakness. While the crystal lattice contains {0k0} cleavage planes that are structurally vulnerable due to the presence of water channels, our results indicate that fracturing perpendicular to the crystal length remains the dominant failure mode under impact. This confirms that for highly acicular materials, the geometric effect of bending is a more powerful driver of attrition than the existence of weak cleavage planes. Collectively, this aerodynamic approach demonstrates its value as a rapid, material-efficient tool for assessing the attrition risk and grindability of fragile pharmaceutical solids.

4. Breakage during Agitated Filter Bed Drying

This study also introduces a novel, laboratory-scale AFBD unit developed as an auxiliary accessory for the FT4 Powder Rheometer, designed to bridge the technology gap in scale-down experimentation by accurately mimicking industrial conditions using minimal material quantities. The experimental prototype features a jacketed 25 mm vessel with interchangeable, 3D-printed impellers that provide precise control over rotational velocity, axial mixing, and temperature (Figure 5).

Figure 5. Experimental setup of the AFBD vessel. [14]

We quantified the extent of breakage (R^*) by measuring the positive shift in particle size distribution as a function of impeller clearance, rotational speed, and environmental conditions. The findings demonstrate that the impeller-base clearance is highly influential, with smaller gaps significantly increasing attrition due to intensified shear deformation in the failure zone. While increasing the number of impeller revolutions expectedly raised the breakage extent, the impeller tip speed within the tested range (0.04 to 0.15 m/s) did not significantly influence breakage for a constant number of rotations (Figures 6a & b). Notably, the application of vacuum suction to consolidate the cake increased the normal load on the powder bed, resulting in a dramatic rise in R^* (Figure 6c). Solvent content emerged as a major factor in particle durability, with crystals breaking more readily at high liquid contents (up to 50% water by mass) due to the formation of capillary bridges that increase inter-particle attraction and resistance to flow (Figure 6d). Shape analysis identified a transition in breakage mechanisms: crystals initially undergo fragmentation by snapping perpendicular to their longest dimension (the (001) plane) and subsequently transition to surface chipping as the particles become smaller and more equant. Ultimately, the study established a linear correlation between the extent of particle breakage and the specific mechanical energy expended by the impeller, confirming the new AFBD unit's value as a comparative assessment tool for optimising industrial drying protocols.

4. Conclusions

This work presents a systematic investigation of particle breakage during agitated filter bed drying using carbamazepine dihydrate as a model fragile pharmaceutical crystal. By combining a laboratory-scale AFBD surrogate with an orthogonal aerodynamic dispersion method, the study successfully disentangled the contributions of shear- and impact-induced attrition. The results demonstrate that particle breakage is a progressive, multi-regime process, transitioning from snapping-driven fragmentation of high-aspect-ratio crystals to surface chipping as particles become more equant.

The newly developed AFBD unit provides a material-efficient and scalable platform that reliably captures the influence of key process variables, including impeller clearance, consolidation load, solvent content, and mechanical energy input. Together with the Morphologi

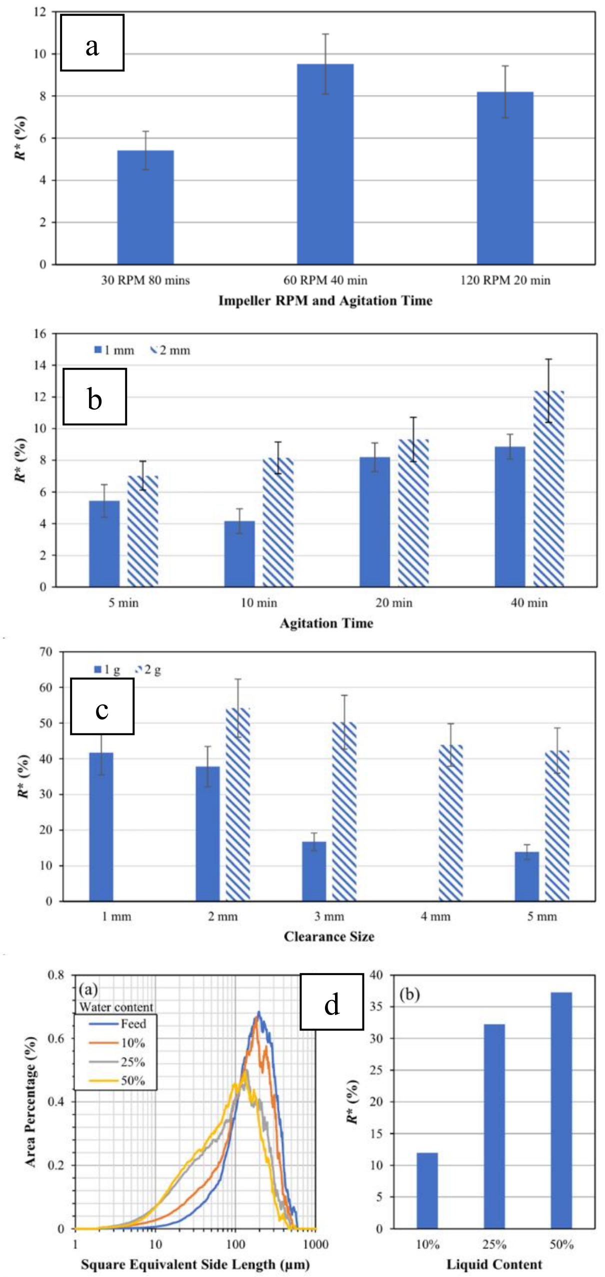

Figure 6. R* as a function of (a) impeller RPM and agitation time (fixed number of rotations), (b) agitation time, (c) clearance size (with vacuum suction) and (d) liquid content. [14]

G3-based impact assessment, this integrated experimental framework offers valuable mechanistic insight into particle degradation during agitated drying and represents a practical toolset for the rational design and optimisation of AFBD processes for mechanically fragile pharmaceutical solids.

References

[1] Bagster, D.F. and Bridgwater, J. (1969) The flow of granular material over a moving blade. *Powder Technol.*, 3(1), 323–338.

[2] Lekhal, A., Girard, K.P., Brown, M.A., Kiang, S., Glasser, B.J. and Khinast, J.G. (2003) Impact of agitated drying on crystal morphology: KCl-water system. *Powder Technol.*, 132(2–3), 119–130.

[3] Lekhal, A., Girard, K.P., Brown, M.A., Kiang, S., Khinast, J.G. and Glasser, B.J. (2004) The effect of agitated drying on the morphology of L-threonine (needle-like) crystals. *Int. J. Pharm.*, 270(1–2), 263–277.

[4] Neil, A.U. and Bridgwater, J. (1994) Attrition of particulate solids under shear. *Powder Technol.*, 80(3), 207–219.

[5] Hare, C., Ghadiri, M. and Dennehy, R. (2011) Prediction of attrition in agitated particle beds. *Chem. Eng. Sci.*, 66(20), 4757–4770.

[6] Remy, B., Kightlinger, W., Saurer, E.M., Domagalski, N. and Glasser, B.J. (2015) Scale-up of agitated drying: Effect of shear stress and hydrostatic pressure on active pharmaceutical ingredient powder properties. *AIChE J.*, 61(2), 407–418.

[7] Tamrakar, A., Gunadi, A., Piccione, P.M. and Ramachandran, R. (2016) Dynamic agglomeration profiling during the drying phase in an agitated filter dyer: Parametric investigation and regime map studies. *Powder Technol.*, 303, 109–123.

[8] Papageorgiou, C.D., Mitchell, C., Quon, J.L., Langston, M., Borg, S., Hicks, F., Ende, D.A. and Breault, M. (2020) Development of a Novel Screening Methodology for the Assessment of the Risk of Particle Size Attrition during Agitated Drying. *Org. Process Res. Dev.*, 24(2), 242–254.

[9] Conder, E.W., Cosbie, A.S., Gaertner, J., Hicks, W., Huggins, S., MacLeod, C.S., Remy, B., Yang, B-S., Engstrom, J.D., Lamberto, D.J. and Papageorgiou, C.D. (2017) The Pharmaceutical Drying Unit Operation: An Industry Perspective on Advancing the Science and Development Approach for Scale-Up and Technology Transfer.

[10] Harris, R.K., Ghi, P.Y., Puschmann, H., Apperley, D.C., Griesser, U.J., Hammond, R.B., Ma, C., Roberts, K.J., Pearce, G.J., Yates, J.R. and Pickard, C.J. (2005) Structural studies of the polymorphs of carbamazepine, its dihydrate, and two solvates. *Org. Process Res. Dev.*, 9(6), 902–910.

[11] Khoo, J.Y., Shah, U.V., Schaepertoens, M., Williams, D.R. and Heng, J.Y.Y. (2013) Process-induced phase transformation of carbamazepine dihydrate to its polymorphic anhydrates. *Powder Technol.*, 236, 114–121.

[12] Rauber, G. (2018) Examination of stress-induced transformations within multicomponent pharmaceutical crystals.

[13] Goh, W.P., Ali, M., Sinha, K., Nere, N.K., Ho, R., Bordawekar, S., Sheikh, A. and Ghadiri, M. (2019) Assessment of impact breakage of carbamazepine dihydrate due to aerodynamic dispersion. *Int. J. Pharm.*, 572, 118780.

[14] Goh, W.P., Sinha, K., Nere, N.K., Ho, R., Bordawekar, S., Sheikh, A. and Ghadiri, M. (2022) Breakage Assessment of Lath-Like Crystals in a Novel Laboratory-Scale Agitated Filter Bed Dryer. *Pharm. Res.*, 39(12), 3209.