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(REVIEW ARTICLE)

Impact of particle size distribution on the degree of compaction and mechanical properties of pharmaceutical tablets: Current perspectives and future trends

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Abstract

The size of constituent particles, together with the breadth of their distribution, is among the most influential material attributes governing how a pharmaceutical powder consolidates into a tablet and how that tablet subsequently performs. Particle dimensions shape powder flow, the efficiency with which a powder bed packs, the residual porosity of the compact and, ultimately, its tensile strength and tendency to recover elastically. Because finer fractions present a greater specific surface area, they tend to form more numerous interparticle contacts and stronger compacts, although powders that are too fine flow poorly and complicate downstream handling. The particle size distribution has been linked to densification rate, mean yield pressure and the strength developed at a given compression pressure. Classical density-pressure relationships, notably the Heckel and Kawakita treatments, remain the standard means of interrogating these mechanisms, while porosity has emerged as a unifying property connecting compaction to disintegration and dissolution. The maturation of Quality by Design, process analytical technology, discrete-element simulation and non-destructive terahertz sensing has sharpened the understanding of size-dependent compaction. This review surveys the fundamentals of particle size and its distribution, methods of particle size analysis, the mechanisms of tablet compaction, the principal compression models, the influence of particle size on powder and tablet properties, industrial applications, enabling technologies, persistent challenges and future directions. A clear understanding of how particle size and the degree of compaction interact remains central to developing robust tablet formulations with consistent mechanical properties and predictable drug release.

Keywords: Particle size distribution; Tablet compaction; Tensile strength; Heckel equation; Kawakita equation; Porosity

1. Introduction

1.1. Overview and importance of particle size in tablets

Compressed tablets remain the dominant oral dosage form, favoured for their portability, dosing accuracy, manufacturing economy and patient acceptance. How a tablet performs is largely set by the physical and mechanical state of the powder presented to the press, and among the many attributes that matter, particle size and its distribution (PSD) stand out because they propagate through almost every stage of processing — conditioning flow, packing, the

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ease of volume reduction, the strength of the resulting bond and the rate of drug release [9,11]. Reducing particle size enlarges the surface available for contact and generally strengthens the compact, yet the same reduction raises cohesion and can degrade flow [15,19]; coarser material flows more freely but offers fewer bonding sites and tends to form weaker tablets [11]. Distribution width matters as much as the central value, since broad distributions encourage segregation and threaten content uniformity [44].

1.2. Compaction behaviour and mechanical properties

Consolidation is a sequence in which particles rearrange, deform elastically and plastically, fracture where they are brittle, and finally bond into a coherent body as voids are eliminated [6]. Materials that flow plastically build extensive contact area and form strong tablets, whereas brittle solids fracture to expose fresh, reactive surfaces that themselves participate in bonding [9,29]. Hardness, friability, tensile strength and porosity all track the PSD and the consolidation history of the powder, and the accompanying changes in porosity govern disintegration and dissolution [41,42].

1.3. Models, recent advances and aim of the review

To make consolidation tractable, density–pressure expressions such as the Heckel and Kawakita equations are widely used to extract plasticity and compressibility parameters [3,4,5]. Contemporary manufacturing increasingly relies on systematic development under Quality by Design, on continuous processing, and on advanced analytics including laser diffraction, terahertz porosity sensing, near-infrared monitoring and numerical simulation [34,39,41,43]. This review consolidates current understanding of how particle size and its distribution shape the degree of compaction and the mechanical performance of tablets, covering the underlying theory, the dominant compression models, established industrial practice, recent instrumentation and the directions the field is taking.

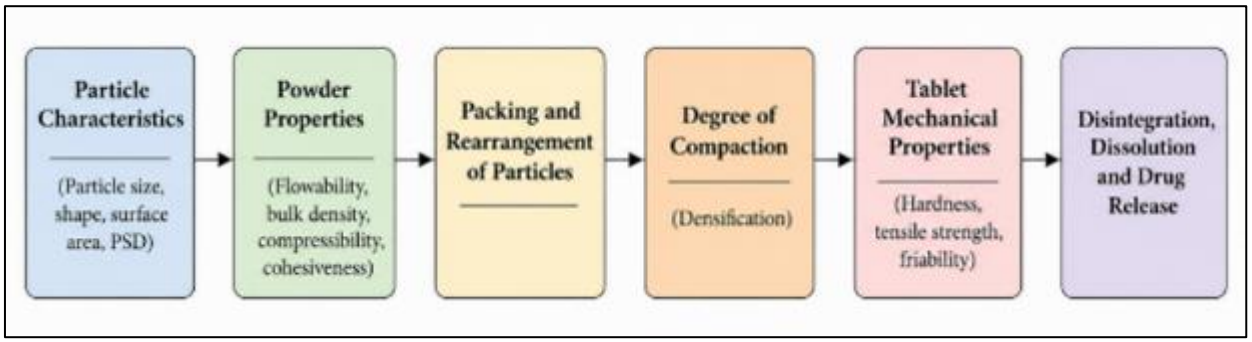


Figure 1 Cascade of factors that link particle characteristics to final tablet quality

2. Fundamentals of Particle Size and Particle Size Distribution

2.1. Particle size and particle size distribution

Particle size is a foundational descriptor of any particulate solid. For the irregular crystals typical of drug substances, it is expressed as an equivalent spherical diameter, and because the answer depends on the measurement, several mean diameters (by number, surface or volume) coexist [9]. Real powders span a range of sizes whose breadth, narrow or broad, monodisperse or polydisperse, governs handling: a tight distribution aids content uniformity and reproducibility, whereas a wide one invites segregation and erratic tablet properties [11,44]. Distribution also dictates packing, as small particles lodge in the interstices between larger ones to raise packing density and lower porosity, although an excess of fines reverses the benefit by increasing cohesion [15].

2.2. Factors affecting size and its pharmaceutical significance

Milling and micronisation are the usual routes to smaller particles, the achievable reduction depending on mill type, energy input and feed brittleness [15], while granulation moves size upward: wet processing yields dense, free-flowing granules and dry routes such as roller compaction can leave a broader, more irregular population [31,33]. Smaller particles expose more surface and can accelerate dissolution of sparingly soluble drugs, but the same increase in surface raises cohesion and can compromise processability; a well-chosen distribution improves die filling, evens out compression, suppresses segregation and bolsters tablet strength while also influencing porosity and release [9,22,41].

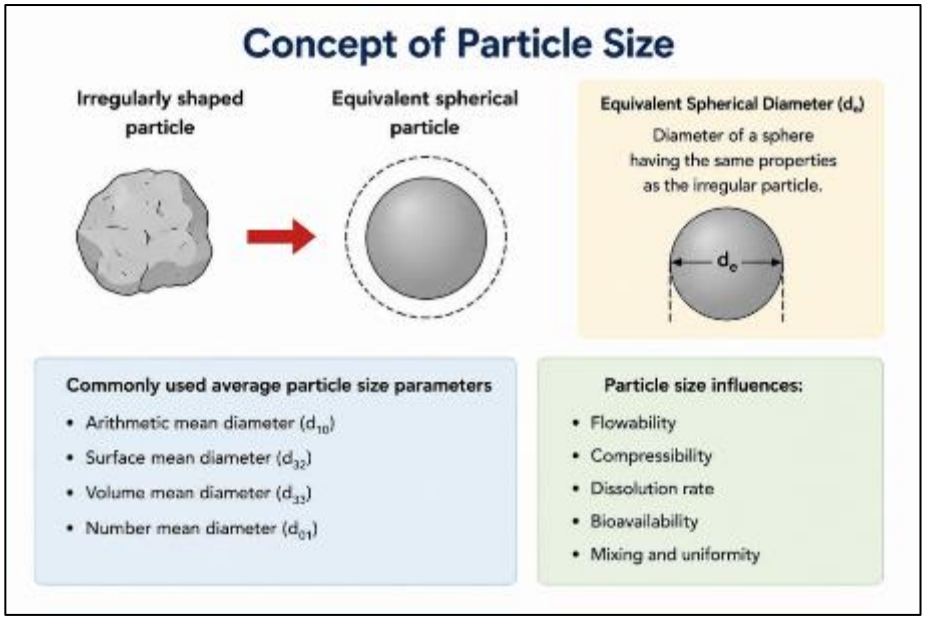
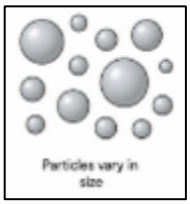


Figure 2 Concept of particle size: an irregular particle, its equivalent spherical diameter and the common average size parameters

Table 1 Classification of particle size distributions

Type of system	Description	Characteristics	Examples
 Monodisperse (uniform)	Particles are of almost the same size.	Narrow distribution; high uniformity; less segregation; reproducible processing.	Spherical beads; crystalline APIs of uniform size.
 Polydisperse (non-uniform)	Particles span a wide range of sizes.	Wide distribution; higher chance of segregation; may improve packing if bimodal.	Crushed materials; milled powders; granules.

A controlled (narrow or bimodal) particle size distribution is generally preferred for better flow, packing and compression.

Table 2 Factors affecting particle size and distribution

Factor	Influence on particle size	Explanation / examples
 Milling / micronization	↓ Decreases particle size	Higher milling speed, longer milling time and suitable equipment reduce particle size.

 Granulation process	↑ Increases particle size (forms granules)	Wet granulation produces larger, denser granules with improved flow.
 Drying conditions	↕ May increase or decrease size	Over-drying may cause shrinkage; high humidity may lead to agglomeration.
 Crystal habit and material properties	↔ Affects shape and size distribution	Hardness, brittleness, elasticity and moisture affect size reduction.
 Environmental conditions	↑ May increase particle aggregation	High humidity and electrostatic charge cause agglomeration of particles.
 Agglomeration	↑ Increases effective particle size	Van der Waals forces, moisture and binding agents cause agglomerates.

Table 3 Significance of particle size in pharmaceutics

Aspect	**Role / importance**
Flowability	Proper particle size improves flow by reducing interparticle cohesion; very fine particles show poor flow.
Compressibility and compactibility	Smaller particles increase surface area and bonding, leading to higher strength; an optimum size gives the best compactibility.
Packing ability	A suitable distribution (e.g., bimodal) improves packing by filling smaller particles into voids between larger ones, reducing porosity.
Dissolution rate	Smaller particles have a larger surface area, leading to faster dissolution and better bioavailability.
Content uniformity	A narrow particle size distribution reduces segregation and improves uniformity in blends.
Tablet quality	Affects hardness, friability, disintegration time and overall performance of tablets.
Manufacturing efficiency	Controlled particle size ensures consistent die filling, reduces weight variation and improves process efficiency.

3. Methods of Particle Size Analysis

3.1. Techniques and their selection

Sizing a powder underpins almost every judgement about its processability, from flow and compressibility to blending and dissolution, and the choice of technique follows from the size range, the material and the question asked. Sieve analysis passes a powder through a nest of sieves of decreasing aperture; it is inexpensive and standardised for coarse material above roughly 50 µm but falters for fine or cohesive powders. Laser diffraction infers size from the angular pattern of scattered light and is valued for speed, wide range and reproducibility, though it assumes sphericity. Dynamic light scattering tracks the Brownian motion of suspended particles to return a hydrodynamic diameter for colloidal and nanoscale systems. Microscopy (optical, SEM, TEM) allows direct visualisation of size, shape and surface texture, while sedimentation derives size from settling velocity through Stokes' law and image analysis couples microscopy with automated software for quantitative shape and size data. Because size touches flow, die filling, consolidation, dissolution and uniformity, its measurement is central to producing good tablets, and a controlled distribution is treated as a critical material attribute within Quality by Design [34,35].

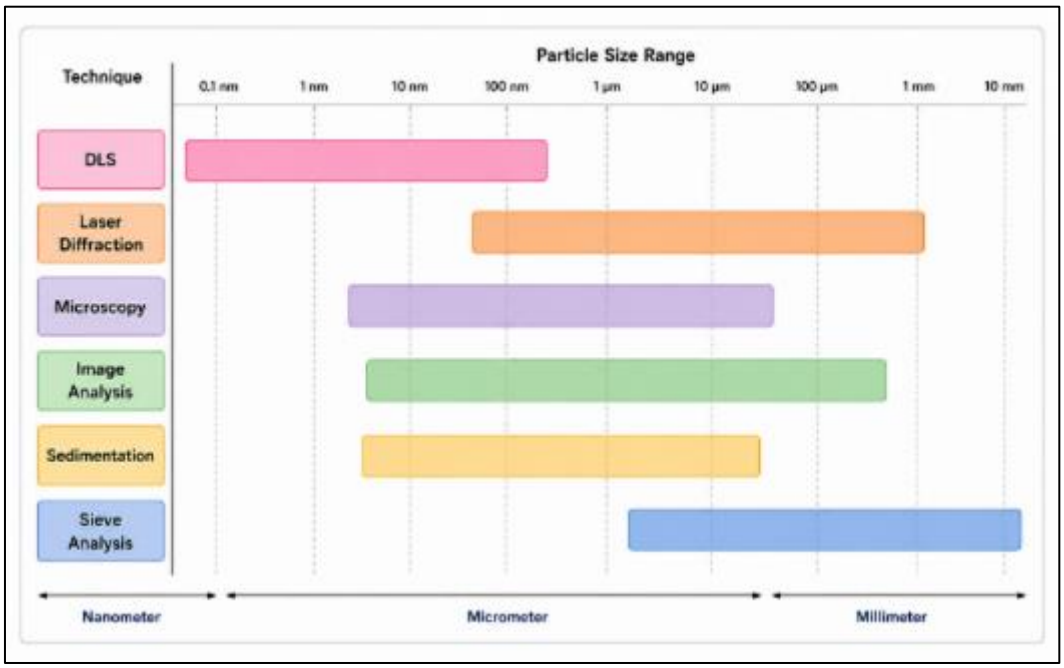
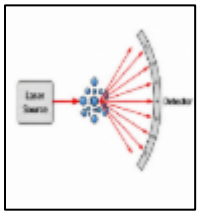
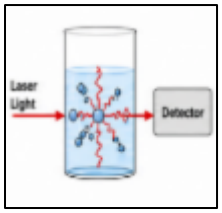
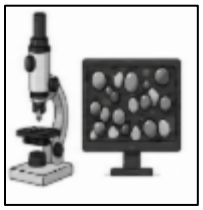
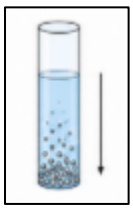


Figure 3 Approximate particle size ranges covered by the different analysis techniques

Table 4 Comparison of particle size analysis techniques.

Method	Principle	Particle size range	Advantages	Limitations	Suitable applications
 Sieve analysis	Separation based on particle size using standard sieves	> 50 µm	Simple, inexpensive, standardized	Not suitable for fine particles; time consuming	Granules, coarse powders, QC testing

 Laser diffraction	Light scattering based on particle size	0.1 µm – 3500 µm	Rapid, wide range, high reproducibility	Expensive; assumes spherical particles	Powders, suspensions, industrial and R&D use
 DLS	Brownian motion of particles in liquid	1 nm – 1 µm	Highly sensitive, small sample requirement	Less accurate for polydisperse samples	Nanoparticles, colloids, liposomes, nanosuspensions
 Microscopy	Direct imaging of particles	0.1 µm – 1000 µm	Provides shape and morphology information	Time consuming; small sample size	Morphology studies, surface analysis, research
 Sedimentation	Settling velocity in a liquid medium	0.5 µm – 1000 µm	Suitable for fine particles, simple	Affected by density and viscosity	Fine powders, suspensions
 Image analysis	Digital analysis of captured images	0.5 µm – 3000 µm	Automated, reduces operator bias	Requires high-quality images; expensive software	Particle shape and size distribution, R&D

4. Fundamentals of Tablet Compaction

4.1. The compression cycle

Compaction is the step in which a loose bed of powder or granules is forced under load into a self-supporting solid of defined strength and uniformity; it is decisive for hardness, porosity, friability and dissolution [18,41]. The press carries the powder through three connected phases — die filling, where adequate flow and a suitable distribution give even fill and consistent weight; compression, where particles rearrange and densify and interparticle bonds develop; and ejection, where excessive friction or rebound can cause capping or lamination.

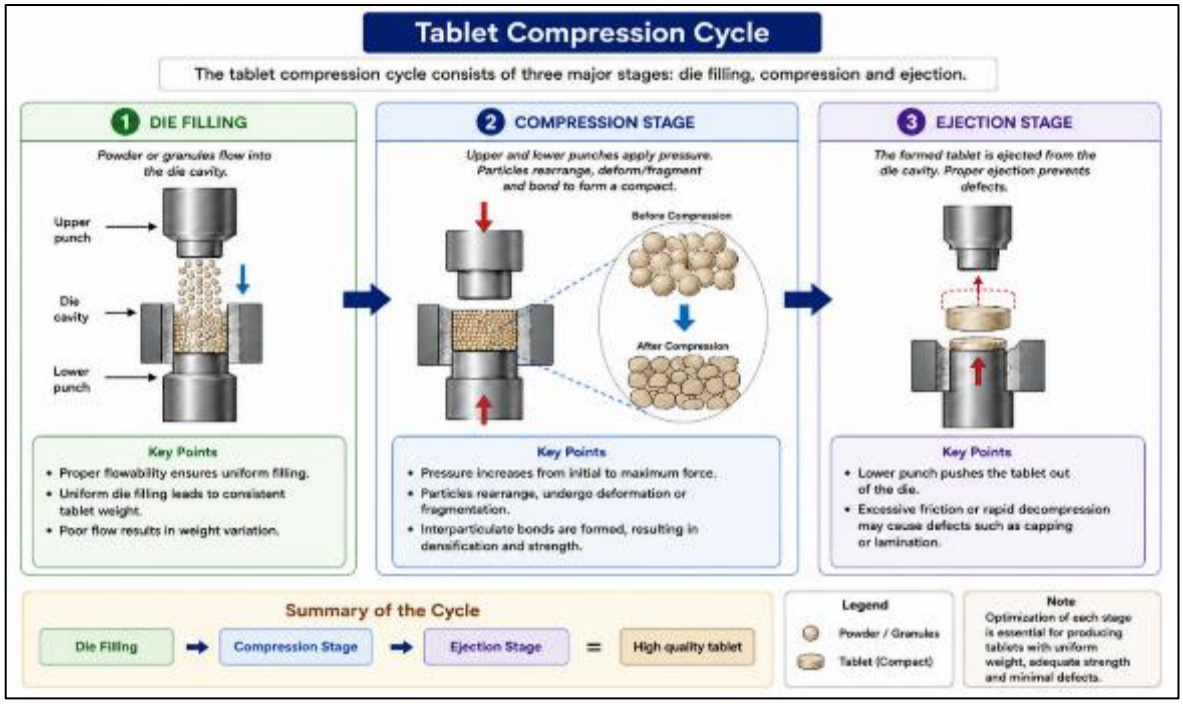


Figure 4 The three-stage tablet compression cycle: die filling, compression and ejection

4.2. Stages of consolidation and bonding

At the particle scale, consolidation unfolds through a recognisable progression: under light load particles rearrange to fill voids; some deform elastically and recover on unloading; plastic flow enlarges the area of true contact and underlies strong bonding, as in microcrystalline cellulose [14,46]; brittle particles fracture to create fresh bonding surfaces; and bonds form through van der Waals attraction, mechanical interlocking and solid bridges [23]. Several variables jointly govern how a powder consolidates (Table 5): particle size, moisture, compression pressure, lubricant level, particle shape and the intrinsic deformation behaviour of the material. Poorly controlled consolidation surfaces as capping, lamination, sticking, picking or weight variation, so systematic compaction study feeds directly into formulation optimisation and the consistent quality that Quality by Design and continuous operation demand [34,36,48].

Table 5 Principal variables influencing the tablet compaction process

Variable	Influence on the compaction process
Particle size	Sets the packing density and the area available for interparticulate bonding.
Moisture content	Modifies particle plasticity and can promote solid-bridge formation.
Compression pressure	Drives densification and dictates the residual porosity of the compact.
Lubricant level	Eases ejection by lowering die-wall friction, but excess can impair bonding.
Particle shape	Alters flow, packing geometry and the degree of mechanical interlocking.
Deformation behaviour	Determines whether bonding proceeds mainly by plastic flow or by fragmentation.

5. Compression Models and Mathematical Approaches

5.1. Heckel, Kawakita and Walker models

Compression models translate force–displacement data into parameters describing rearrangement, deformation, densification and bonding. The Heckel relationship frames pore elimination as first-order in applied pressure; the reciprocal of its slope, the mean yield pressure, indexes plasticity, with lower values signalling more readily deforming, better-compacting solids [3,4,26], though it behaves poorly at low pressure and for elastic materials [25]. The Kawakita

expression describes the degree of volume reduction as a function of pressure and is best suited to low-pressure regimes and loose, cohesive powders, with parameters linked to initial bed voidage and particle failure, making it a sensitive probe of rearrangement [5,12]. The older Walker treatment relates compact volume to the logarithm of applied pressure and supplies a compressibility coefficient for ranking materials [7].

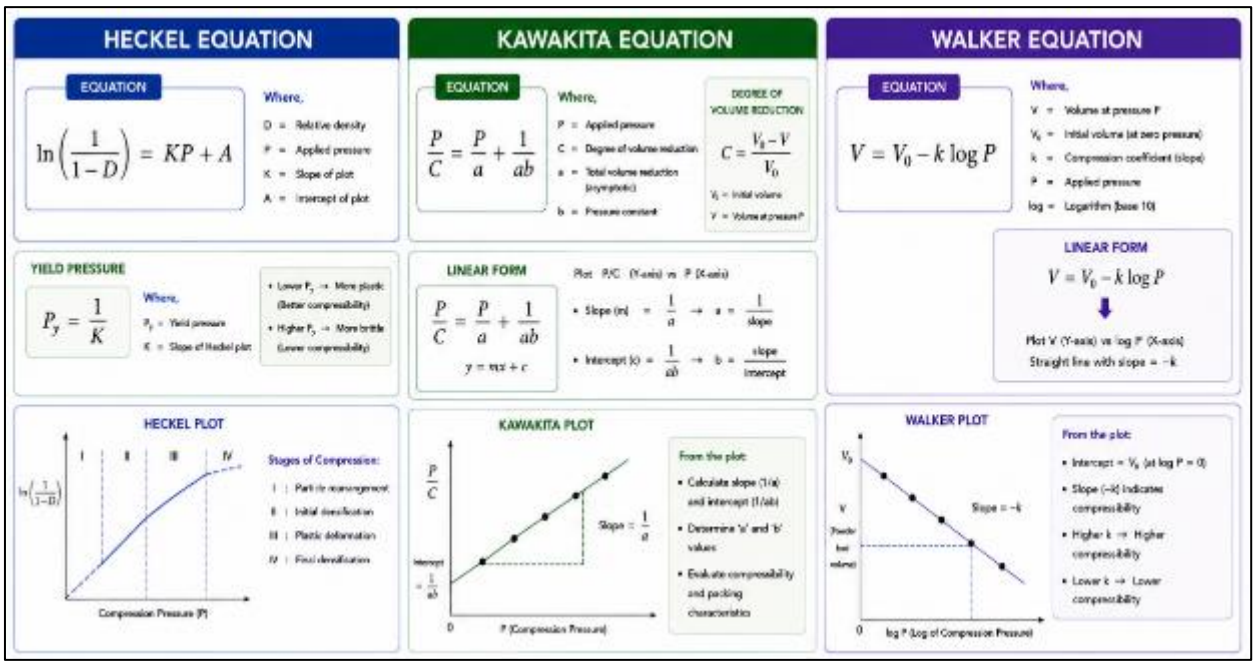


Figure 5 The common powder compaction models

5.2. Compressibility and compactibility

It is worth distinguishing compressibility, the readiness of a powder to lose volume under load, from compactibility, its ability to translate that volume change into mechanical strength [20,49]. Both respond to size, shape, moisture, deformation mode and pressure; fine powders generally compact better thanks to their larger surface and denser contact network, subject to the usual penalty in flow [9,10,11]. Used judiciously, these models help select excipients, characterise deformation, predict strength, forestall defects and smooth scale-up within a Quality by Design framework [34,47].

6. Effect of Particle Size on Powder Properties

6.1. Flow, density and packing

Size and distribution leave their imprint on flow, packing, density, compressibility, cohesion and segregation. Coarser powders flow more readily because lower surface area weakens interparticle attraction, whereas fine powders are dominated by cohesion and flow sluggishly [11]; empirical indices such as the Carr index and Hausner ratio summarise this behaviour. Bulk density reflects as-poured packing and tapped density packing after settling: small particles can infiltrate gaps between larger ones to raise density, while strongly cohesive fines may trap air and lower it. A blend spanning a sensible range of sizes packs efficiently, lowering porosity and strengthening the compact, but wide distributions separate during handling to undermine content uniformity [44].

6.2. Cohesion and compressibility

Fine particles cohere more strongly through van der Waals and electrostatic forces [15] and usually compress more readily because their greater surface promotes bonding [9,10]; beyond an optimum, however, they invite sticking, poor flow and over-densification, while very coarse material bonds weakly, so a balanced distribution is the practical goal. Controlling the distribution improves blending, handling, compression, uniformity and reproducibility, which is why particle engineering and Quality by Design are now routine in optimising powder behaviour [19,34].

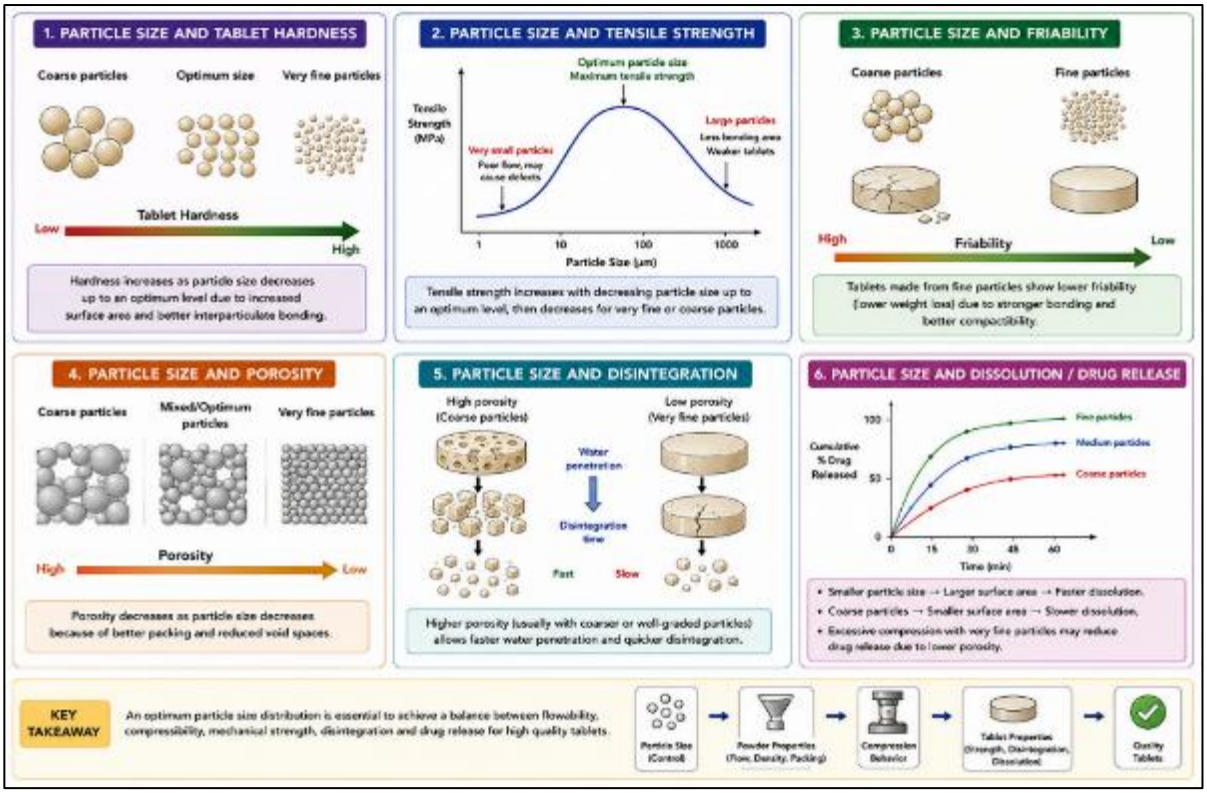


Figure 6 How particle size influences hardness, tensile strength, friability, porosity, disintegration and dissolution

7. Influence of Particle Size on Compaction Mechanisms

7.1. Deformation, fracture and elastic recovery

Under load, particles rearrange, deform, fracture and bond, and the relative weight of each depends on size, shape and intrinsic mechanical character [9,10]. Plastic flow creates the large contact areas on which strong bonding depends, with microcrystalline cellulose the textbook example [14,46]; finer particles deform and reorganise more effectively, though excessive comminution raises cohesion and undermines flow. Brittle solids such as lactose fracture rather than flow, and the new surfaces add bonding area and aid densification, their strength depending largely on the degree of fragmentation [29]. Recovery on unloading can fracture a freshly formed compact, producing capping, lamination or cracking, an effect tied to compression speed and dwell time [13,16].

7.2. Rearrangement, bonding and densification

At low pressure the bed mainly repacks, fines slipping into voids to raise packing efficiency and lower porosity [12], the very rearrangement the Kawakita parameters are sensitive to. Fragments expose clean surfaces that bond through van der Waals forces, solid bridges, interlocking and electrostatic attraction, so more fines mean more bonding area and stronger tablets until sticking and flow problems set the limit [23,44]. Overall, fine powders consolidate to lower porosity and higher relative density, giving stronger tablets, whereas coarse material resists densification through limited contact and inefficient packing [9,10]. A working knowledge of these mechanisms guides excipient choice, pressure setting and defect control, and supports both Quality by Design and continuous manufacturing [34,47].

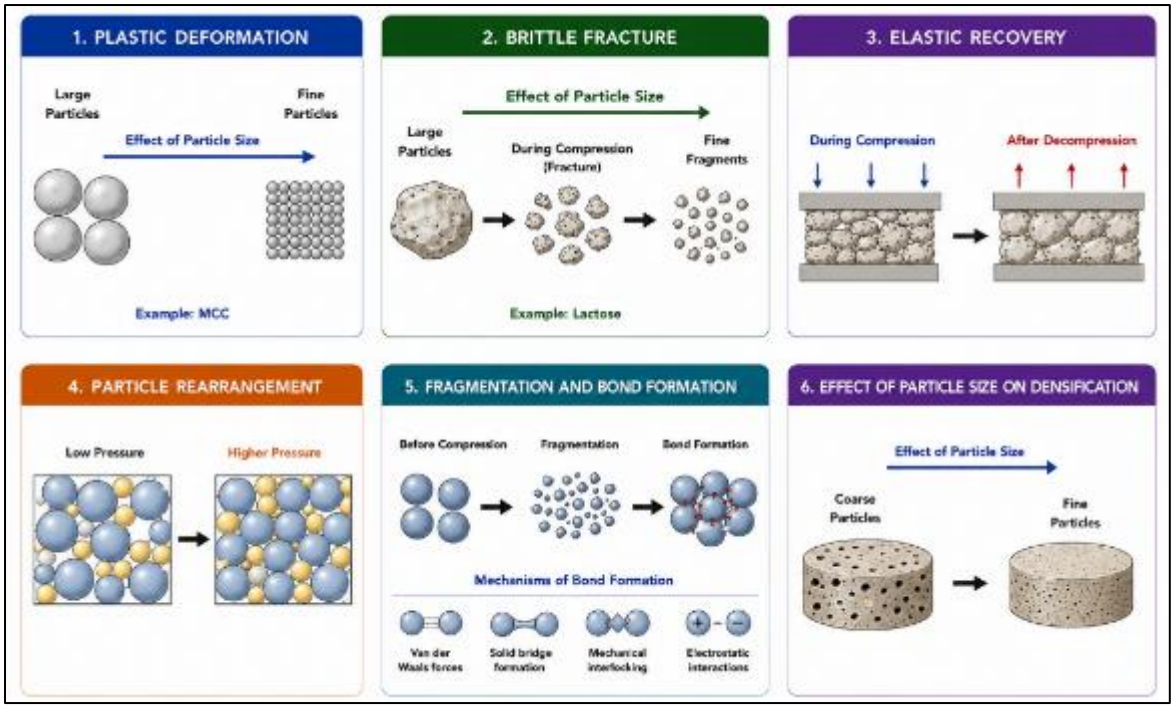


Figure 7 Compaction mechanisms and their response to particle size: plastic deformation, brittle fracture, elastic recovery, rearrangement, bond formation and densification

8. Industrial and Pharmaceutical Applications

8.1. Compression and granulation routes

Direct compression presses the blend straight into tablets without granulation and so demands excellent flow, compressibility and uniformity; because fines strengthen while coarse material flows, the distribution must be tuned to satisfy both [9,11], with microcrystalline cellulose the mainstay filler-binder owing to its plasticity [14,46]. Wet granulation agglomerates particles with a liquid binder to build larger, free-flowing granules, improving packing, compressibility and uniformity and favoured for cohesive, poorly flowing or low-dose materials. Where moisture or heat must be avoided, dry granulation by slugging or roller compaction densifies the powder without liquid [31], though a recognised drawback is the loss of tabletability that accompanies size enlargement, since pre-compacted granules bond less readily than the original powder [30,32].

8.2. Continuous manufacturing, scale-up and particle engineering

In continuous lines, material moves without interruption through linked unit operations, so size control directly governs feeding, blending and compression [36,38], with inline near-infrared and related analytics tracking size and consolidation in real time [37,39,40]. Carrying a process from bench to plant requires that distribution and consolidation behaviour hold steady, since changes in equipment, speed, blending and granulation can shift particle attributes and faster presses in particular alter the yield pressure of plastic materials [13,16]. Milling, micronisation, granulation, spray drying and controlled crystallisation are all deployed to tailor powder properties, with Quality by Design used to fix the optimal size window [19,34].

Figure 8 Industrial contexts: direct compression, wet and dry granulation, continuous manufacturing, scale-up and particle engineering

9. Advanced Technologies and Recent Developments

9.1. PAT and Quality by Design

Process analytical technology brings real-time measurement to critical parameters — size, blend uniformity, compression force and moisture — so that processes can be steered rather than merely inspected [34,39], with near-infrared and Raman spectroscopy the most widely deployed sensors [39,40]. Quality by Design develops products against predefined quality targets [34,35], treating the size distribution as a critical material attribute and compression force and speed as critical process parameters.

9.2. Modelling, AI and terahertz sensing

Data-driven models increasingly predict flow, compressibility, dissolution and strength from material descriptors, shortening development [50], while discrete-element and finite-element simulation resolve particle-scale rearrangement, densification, stress transmission and die filling, with notable success for roller compaction [43]. Terahertz sensing measures porosity, pore structure, density and coating thickness without destroying the tablet, and because porosity controls mass transport it can anticipate disintegration and dissolution in line [41,42].

10. Challenges and Limitations

10.1. Flow, defects, scale-up and stability

The cohesion accompanying a large surface area can leave fine powders flowing poorly, with consequences for die filling, weight control and handling [11,15]. Fine or damp material may adhere to punch faces and die walls, marring surfaces and slowing production; wide distributions separate during blending and transport to undermine content uniformity [44]. Behaviour established in the laboratory need not survive transfer to production, where larger equipment, faster speeds and altered particle interactions can shift hardness, friability and dissolution [13,16]. Smaller particles also take up moisture and react at their surfaces more readily, making them more liable to clumping, degradation, flow loss and instability on storage. Common compression defects, their causes and control measures are summarised in Table 6.

Table 6 Common tablet compression defects, their causes and control measures

Defect	Appearance	Description	Possible causes	Prevention / control measures
Capping		The top or bottom portion of the tablet separates horizontally from the main body.	Entrapped air; rapid decompression; excess fines; inadequate lubrication; too much binder.	Optimize compression speed; improve powder flow; adjust compression pressure; use adequate lubricant; optimize granulation.
Lamination		Tablet separates into two or more layers.	Entrapped air; high compression pressure; poor particle bonding; improper granulation.	Reduce compression pressure; optimize moisture content; improve granule strength; use a suitable binder.
Sticking		Tablet material adheres to the punch face or die wall.	High moisture content; inadequate lubrication; low-melting excipients; rough punch surface.	Reduce moisture content; use effective lubricant; use anti-adherent agents; polish punch and die surfaces.
Picking		Particles are pulled out of the tablet surface during ejection.	Sticking of material; high moisture content; inadequate lubrication; rough die or punch surface.	Optimize moisture content; improve lubrication; use suitable excipients; polish tooling surfaces.
Cracking		Visible cracks appear on the tablet surface.	Excessive compression pressure; poor plasticity; high elastic recovery; rapid decompression.	Adjust compression force; use a more plastic material; reduce elastic recovery; optimize compression speed.

11. Future Perspectives

11.1. Smart manufacturing, AI and personalised medicine

Smart manufacturing systems integrating real-time sensing, automation and closed-loop feedback are expected to tighten reproducibility and reduce variability [36,38]. Predictive artificial-intelligence and machine-learning models will increasingly forecast flow, compressibility, dissolution and strength, cutting experimental trials [50], while advanced particle engineering — spray drying, nanoengineering, controlled crystallisation and surface modification — will improve compactibility, dissolution and manufacturability [19]. Digital-twin models can predict tablet behaviour across conditions to optimise pressure, distribution and reproducibility [43], and patient-specific dosage forms supported by techniques such as 3D printing will make precise control of size and consolidation more important still.

12. Conclusion

Particle size and the degree of compaction govern the quality, performance and manufacturability of tablets. The distribution sets flow, packing, compressibility, densification and the strength of the bonds that form under pressure; finer fractions generally raise compactibility, tensile strength and hardness through their larger surface and denser contact [9,15,22], while coarser material flows more freely, so reconciling the two is the central formulation compromise. The Heckel, Kawakita and Walker treatments continue to illuminate deformation and densification [3,5,7], and Quality by Design, process analytical technology, simulation and data-driven methods have deepened the picture [34,41,50]. Persistent obstacles — poor flow, segregation, sticking and scale-up variability — keep the subject practically urgent, and a firm understanding of how size and consolidation interact remains the key to robust formulations with consistent mechanics and predictable release.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflicts of interest.

Author Contributions

Author 1, Author 2, Author 3, and Author 4: Conceptualization, literature search, data collection, writing – original draft, visualization, and manuscript editing.

Author 5 and Author 6: Draft editing, supervision, scientific guidance, critical review of the manuscript and editing, final approval of the manuscript.

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Ethics Statement

The authors have nothing to report.

Declaration of Generative AI And AI-Assisted Technologies in the Manuscript Preparation Process

In preparing this manuscript, the authors made use of ChatGPT (OpenAI) for support with language refinement, correction of grammar, organisation of content, and the conceptualisation of figures. Following this use, the authors examined, edited, and revised the material as required, and they accept full responsibility for the content of the publication.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

[1] Fell JT, Newton JM. The tensile strength of lactose tablets. J Pharm Pharmacol. 1968;20(8):657-659.

[2] Fell JT, Newton JM. Determination of tablet strength by the diametral-compression test. J Pharm Sci. 1970;59(5):688-691.

[3] Heckel RW. Density-pressure relationships in powder compaction. Trans Metall Soc AIME. 1961; 221:671-675.

[4] Heckel RW. An analysis of powder compaction phenomena. Trans Metall Soc AIME. 1961; 221:1001-1008.

[5] Kawakita K, Ludde KH. Some considerations on powder compression equations. Powder Technol. 1971;4(2):61-68.

[6] Hersey JA, Rees JE. Deformation of particles during briquetting. Nat Phys Sci. 1971; 230:96.

[7] Walker EE. The properties of powders. Part VI. The compressibility of powders. Trans Faraday Soc. 1923; 19:73-82.

[8] Hersey JA, Rees JE. The effect of particle size on the consolidation of powders during compaction. In: Particle Size Analysis. London: Society for Analytical Chemistry; 1970.

[9] Sun CC, Grant DJW. Effects of initial particle size on the tableting properties of L-lysine monohydrochloride dihydrate powder. Int J Pharm. 2001;215(1-2):221-228.

[10] Patel S, Kaushal AM, Bansal AK. Effect of particle size and compression force on compaction behavior and derived mathematical parameters of compressibility. Pharm Res. 2007;24(1):111-124.

[11] Kaerger JS, Edge S, Price R. Influence of particle size and shape on flowability and compactibility of binary mixtures of paracetamol and microcrystalline cellulose. Eur J Pharm Sci. 2004;22(2-3):173-179.

[12] Nordstrom J, Welch K, Frenning G, Alderborn G. On the physical interpretation of the Kawakita and Adams parameters derived from confined compression of granular solids. Powder Technol. 2008;182(3):424-435.

[13] Tye CK, Sun CC, Amidon GE. Evaluation of the effects of tableting speed on the relationships between compaction pressure, tablet tensile strength, and tablet solid fraction. J Pharm Sci. 2005;94(3):465-472.

[14] Roberts RJ, Rowe RC, York P. The relationship between the fracture properties, tensile strength and critical stress intensity factor of organic solids and their molecular structure. Int J Pharm. 1995;125(1):157-162.

[15] Khan F, Pilpel N. The effect of particle size and moisture on the tensile strength of microcrystalline cellulose powder. Powder Technol. 1986;48(2):145-150.

[16] Roberts RJ, Rowe RC. The effect of punch velocity on the compaction of a variety of materials. J Pharm Pharmacol. 1985;37(6):377-384.

[17] Hiestand EN, Smith DP. Indices of tableting performance. Powder Technol. 1984;38(2):145-159.

[18] Hiestand EN. Mechanical properties of compacts and particles that control tableting success. J Pharm Sci. 1997;86(9):985-990.

[19] Sun CC. Decoding powder tabletability: roles of particle adhesion and plasticity. J Adhes Sci Technol. 2011;25(4-5):483-499.

[20] Leuenberger H. The compressibility and compactibility of powder systems. Int J Pharm. 1982;12(1):41-55.

[21] Alderborn G, Nystrom C, eds. Pharmaceutical Powder Compaction Technology. New York: Marcel Dekker; 1996.

[22] Sebhatu T, Alderborn G. Relationships between the effective interparticulate contact area and the tensile strength of tablets of amorphous and crystalline lactose of varying particle size. Eur J Pharm Sci. 1999;8(4):235-242.

[23] Nystrom C, Alderborn G, Duberg M, Karehill PG. Bonding surface area and bonding mechanism: two important factors for the understanding of powder compactability. Drug Dev Ind Pharm. 1993;19(17-18):2143-2196.

[24] Denny PJ. Compaction equations: a comparison of the Heckel and Kawakita equations. Powder Technol. 2002;127(2):162-172.

[25] Sonnergaard JM. A critical evaluation of the Heckel equation. Int J Pharm. 1999;193(1):63-71.

[26] Gabaude CMD, Guillot M, Gautier JC, Saudemon P, Chulia D. Effects of true density, compacted mass, compression speed, and punch deformation on the mean yield pressure. J Pharm Sci. 1999;88(7):725-730.

[27] Kuentz M, Leuenberger H. Pressure susceptibility of polymer tablets as a critical property: a modified Heckel equation. J Pharm Sci. 1999;88(2):174-179.

[28] Newton JM, Grant DJW. The relation between the compaction pressure, porosity and tensile strength of compacted powders. Powder Technol. 1974;9(5-6):295-297.

[29] Roberts RJ, Rowe RC. Brittle/ductile behaviour in pharmaceutical materials used in tabletting. Int J Pharm. 1987;36(2-3):205-209.

[30] Sun CC, Himmelspach MW. Reduced tabletability of roller compacted granules as a result of granule size enlargement. J Pharm Sci. 2006;95(1):200-206.

[31] Kleinebudde P. Roll compaction/dry granulation: pharmaceutical applications. Eur J Pharm Biopharm. 2004;58(2):317-326.

[32] Sun CC, Kleinebudde P. Mini review: mechanisms to the loss of tabletability by dry granulation. Eur J Pharm Biopharm. 2016; 106:9-14.

[33] Herting MG, Kleinebudde P. Roll compaction/dry granulation: effect of raw material particle size on granule and tablet properties. Int J Pharm. 2007;338(1-2):110-118.

[34] Yu LX. Pharmaceutical Quality by Design: product and process development, understanding, and control. Pharm Res. 2008;25(4):781-791.

[35] Yu LX, Amidon G, Khan MA, et al. Understanding pharmaceutical quality by design. AAPS J. 2014;16(4):771-783.

[36] Lee SL, O'Connor TF, Yang X, et al. Modernizing pharmaceutical manufacturing: from batch to continuous production. J Pharm Innov. 2015;10(3):191-199.

[37] Fonteyne M, Soares S, Vercruysse J, et al. Prediction of quality attributes of continuously produced granules using complementary PAT tools. Eur J Pharm Biopharm. 2012;82(2):429-436.

[38] Portier C, Vervaet C, Vanhoorne V. Continuous twin screw granulation: a review of recent progress and opportunities in formulation and equipment design. Pharmaceutics. 2021;13(5):668.

[39] Roggo Y, Chalus P, Maurer L, Lema-Martinez C, Edmond A, Jent N. A review of near infrared spectroscopy and chemometrics in pharmaceutical technologies. J Pharm Biomed Anal. 2007;44(3):683-700.

[40] Vanarase AU, Alcala M, Jerez Rozo JI, Muzzio FJ, Romanach RJ. Real-time monitoring of drug concentration in a continuous powder mixing process using NIR spectroscopy. Chem Eng Sci. 2010;65(21):5728-5733.

[41] Bawuah P, Markl D, Turner A, et al. A fast and non-destructive terahertz dissolution assay for immediate release tablets. J Pharm Sci. 2021;110(6):2083-2092.

[42] Markl D, Strobel A, Schlossnikl R, et al. Characterisation of pore structures of pharmaceutical tablets: a review. Int J Pharm. 2018;538(1-2):188-214.

[43] Muliadi AR, Litster JD, Wassgren CR. Modeling the powder roll compaction process: comparison of 2-D finite element method and the rolling theory for granular solids (Johanson's model). Powder Technol. 2012; 221:90-100.

[44] Yohannes B, Gonzalez M, Abebe A, et al. The role of fine particles on compaction and tensile strength of pharmaceutical powders. Powder Technol. 2016; 290:62-70.

[45] Persson AS, Alderborn G. Tabletability and compactibility of alpha-lactose monohydrate powders of different particle size. Pharm Dev Technol. 2018;23(3):227-237.

[46] Joiris E, Di Martino P, Berneron C, Guyot-Hermann AM, Guyot JC. Compression behavior of orthorhombic paracetamol. Pharm Res. 1998;15(7):1122-1130.

[47] Sun CC. Materials science tetrahedron: a useful tool for pharmaceutical research and development. J Pharm Sci. 2009;98(5):1671-1687.

[48] Akseli I, Ladyzhynsky N, Katz J, He X. Development of predictive tools to assess capping tendency of tablet formulations. Powder Technol. 2013; 236:139-148.

[49] Paul S, Sun CC. The suitability of common compressibility equations for characterizing plasticity of diverse powders. Int J Pharm. 2017;532(1):124-130.

[50] Vreeman G, Sun CC. Mean yield pressure from the in-die Heckel analysis is a reliable plasticity parameter. Int J Pharm X. 2021; 3:100094.