INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Microcrystalline Cellulose in Direct Compression: Material Attributes, Compaction Behavior, and Tablet Performance

Harshwardhan Lohar*[1], Avantika Mane[2], Vinayak Patil[3], Jayant Patil[4]

[1] *Department of Pharmaceutics, Arvind Gavali College of Pharmacy, Jaitapur, Satara, Maharashtra, India*
[2] *Department of Pharmaceutics, Tatyasaheb Kore College of Pharmacy, Warananagar, Maharashtra, India*
[3] *Department of Pharmaceutical Quality Assurance, Adarsh College of Pharmacy, Vita, Maharashtra, India*
[4] *Department of Pharmaceutical Quality Assurance, Vasantidevi Patil Institude of Pharmacy, Kodoli, Maharashtra, India*

ARTICLE INFO

Published: 26 Aug 2026
Keywords:
Microcrystalline Cellulose, Direct Compression, Tabletability, Critical Material Attributes, Excipient Functionality, Tablet Performance
DOI:
10.5281/zenodo.22120642

ABSTRACT

Direct compression (DC) is an efficient tablet manufacturing technique in which a powder blend containing the active pharmaceutical ingredient (API) and suitable excipients is compressed directly without an intermediate granulation step. Although DC offers advantages such as reduced processing time, lower energy consumption, fewer manufacturing operations, and limited exposure to heat and moisture, it requires excipients with appropriate flow and compaction properties. Microcrystalline cellulose (MCC) is one of the most widely used excipients in DC formulations because of its excellent compactibility, tabletability, dry-binding capacity, and favorable plastic deformation behavior. However, MCC performance is influenced by several material attributes, including particle size, particle-size distribution, morphology, porosity, density, moisture content, crystallinity, surface characteristics, and manufacturing conditions. This review critically examines the physicochemical and functional properties of MCC and their relationship with direct-compression performance. Particular emphasis is placed on MCC deformation and interparticle bonding mechanisms, compressibility, compactibility, tabletability, grade and source variability, lubricant sensitivity, and effects on tablet critical quality attributes. The review also discusses MCC-based co-processed excipients as an emerging approach to improve powder flow, compaction, multifunctionality, and formulation robustness. Furthermore, current developments in advanced material characterization, predictive formulation development, continuous manufacturing, and science-based excipient selection are highlighted. Understanding the relationships among MCC material attributes, powder behavior, compression mechanisms, and final tablet performance is essential for rational

***Corresponding Author:** Harshwardhan Lohar
Address: *Arvind Gavali College of Pharmacy, Jaitapur, Satara, Maharashtra, India*
Email ✉: loharharshwardhan4@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

excipient selection and development of robust direct-compression formulations. Overall, MCC remains a critical multifunctional excipient for modern tablet manufacturing, while continued material engineering and predictive approaches may further enhance its performance and formulation versatility.

INTRODUCTION

Direct compression (DC) is one of the simplest and most widely used approaches for pharmaceutical tablet manufacturing. In this process, the active pharmaceutical ingredient (API) is blended with suitable excipients and compressed directly into tablets without intermediate granulation or drying. Compared with wet granulation, DC offers several advantages, including fewer manufacturing operations, reduced processing time and energy consumption, lower equipment requirements, and limited exposure of formulation components to heat and moisture [1]. However, the absence of a granulation step places greater demands on powder properties. Adequate flowability, packing, compressibility, compactibility, and tabletability are essential for consistent die filling and successful tablet formation. Poor flow can cause tablet-weight variation, whereas inadequate compactibility or tabletability may result in weak tablets, increased friability, capping, or lamination. Particle size, density, morphology, surface characteristics, and moisture content can further influence segregation and tablet performance [2].

Microcrystalline cellulose (MCC) is a purified, partially depolymerized cellulose excipient and one of the most widely used functional excipients in DC formulations. It is primarily used as a diluent and dry binder because of its excellent compaction properties and ability to produce mechanically robust tablets. During compression, MCC undergoes substantial plastic deformation, allowing particles to conform to adjacent particles and establish extensive interparticulate contact. This increases the effective bonding area and promotes strong interparticle bonds, thereby enhancing tablet tensile strength and reducing friability. MCC is particularly valuable in formulations containing APIs with poor compactibility or limited tableting performance [3,4]. Its favorable deformation behavior and ability to facilitate tablet formation have contributed to its widespread use in direct-compression formulations.

The functionality of MCC is strongly influenced by its physicochemical and structural material attributes. Important attributes include particle size and distribution, morphology, porosity, density, moisture content, crystallinity, degree of polymerization, specific surface area, and surface characteristics. These properties can affect powder flow, packing efficiency, deformation behavior, interparticle bonding, and ultimately tablet performance. Particle size and morphology may influence flowability and die filling, whereas porosity and density can affect particle rearrangement, deformation, and bonding during compression. Moisture content may alter interparticle interactions and the mechanical response of MCC, while crystallinity and molecular structure can influence deformation and bonding. Consequently, MCC grades from different manufacturers or production processes may exhibit distinct functional performance despite meeting general compendial specifications. Differences in particle size, moisture content, density, porosity, and surface properties have been associated with variations in powder behavior and tabletability [5,6].

The increasing emphasis on critical material attributes (CMAs), process understanding, continuous manufacturing, and excipient engineering has further highlighted the importance of controlling MCC functionality [7]. Identification

of relevant CMAs can help establish relationships between MCC properties, processing behavior, and critical quality attributes of the resulting tablets. Co-processed MCC-based excipients have also been developed to combine the favorable compaction characteristics of MCC with complementary properties such as improved flowability, enhanced disintegration, reduced lubricant sensitivity, or multifunctionality. Such engineered excipients can address limitations associated with conventional MCC and provide greater formulation flexibility, particularly for challenging APIs and high-drug-load formulations. In addition, lubrication, blending conditions, compression pressure, and dwell time can influence the deformation and bonding behavior of MCC. Therefore, MCC functionality should be considered as an interaction between material attributes, formulation composition, and manufacturing conditions [8].

Although previous reviews have extensively discussed MCC and its application in direct compression, continuing advances in excipient engineering, material characterization, powder technology, and pharmaceutical manufacturing warrant an updated and critically focused assessment. A comprehensive understanding of the relationships among MCC material attributes, powder behavior, deformation mechanisms, compressibility, compactibility, tabletability, and final tablet quality remains important for rational excipient selection and formulation development [5]. Accordingly, this review critically examines the role of MCC in direct-compression tablet manufacturing, focusing on its physicochemical and functional attributes, powder behavior, compression and deformation mechanisms, compressibility, compactibility and tabletability, grade-to-grade variability, lubricant sensitivity, co-processed excipients, and influence on tablet performance. Current research gaps and future opportunities in MCC characterization, functional excipient development, co-processing, and advanced tablet manufacturing are also discussed.

Comprehensive Literature Search

A comprehensive literature search was conducted using PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar to identify relevant literature on Microcrystalline Cellulose, Direct Compression, Tabletability, Critical Material Attributes, Excipient Functionality, and Tablet Performance. Priority was given to peer-reviewed original research articles, review articles, and authoritative pharmaceutical sources. The retrieved literature was critically evaluated with emphasis on the relationships between MCC material attributes, direct-compression behavior, tabletability, critical material attributes, excipient functionality, and overall tablet performance. Relevant studies published in these areas were considered to provide a comprehensive and contemporary assessment of the role of MCC in direct-compression tablet manufacturing.

Direct Compression: Principles and Manufacturing Process

Direct compression is a tablet manufacturing technique in which a powder blend containing the active pharmaceutical ingredient (API) and suitable excipients is compressed directly into tablets without an intermediate granulation step. The process generally involves raw-material dispensing, sieving or particle-size adjustment when necessary, blending, lubrication, compression, and subsequent tablet handling and packaging. The principal advantage of direct compression is the reduction in processing steps compared with conventional wet granulation. The absence of granulation and drying can reduce manufacturing time, energy consumption, equipment requirements, and exposure of

formulation components to moisture and elevated temperatures. Direct compression is therefore particularly advantageous for moisture-sensitive and heat-sensitive pharmaceutical materials and provides a simpler and more efficient manufacturing approach [9].

However, eliminating the granulation step places greater demands on the intrinsic properties of the powder formulation. During wet or dry granulation, poorly flowing or poorly compactable powders can be converted into granules with improved flow, packing, and handling characteristics. Such modification is absent in direct compression, making the inherent properties of APIs and excipients important determinants of manufacturing performance. Adequate flowability is essential for uniform die filling, while compressibility, compactibility, and tabletability influence powder consolidation and the mechanical strength of the resulting tablets [10]. Therefore, appropriate excipient selection and control of critical material attributes are essential for achieving consistent and reproducible direct-compression tablet manufacturing.

1. Manufacturing Process [11]

The general sequence can be represented as:

Raw material dispensing → Sieving/milling, if required → Pre-blending → Final blending → Lubrication → Compression → Dedusting and inspection → Packaging

Particle-size adjustment may be performed when required to improve blend uniformity or flow. The API and excipients are subsequently blended to obtain a homogeneous powder mixture. Lubrication is generally performed after blending by incorporating an appropriate lubricant under controlled mixing conditions. The lubricated blend is transferred to the tablet compression machine, where it is compacted under controlled pressure.

2. Advantages [12]

Direct compression provides:

- Reduced manufacturing operations
- Shorter processing time
- Lower energy consumption
- Reduced equipment requirements
- Reduced exposure to heat and moisture
- Lower potential for processing-related degradation
- Simplified process control
- Potential reduction in manufacturing cost
- Suitability for high-throughput manufacturing
- Potential compatibility with continuous manufacturing

3. Limitations

The major limitation of direct compression is its dependence on the intrinsic properties of the powder blend. Poor flowability may result in inadequate die filling, whereas differences in particle size, density, or morphology may cause segregation. Poor compressibility or compatibility may result in insufficient tablet strength, while excessive elastic recovery may contribute to capping and lamination. Lubricant concentration, blending time, compression force, compression speed, moisture content, and excipient grade may further influence tablet performance [13].

Table 1. Comparison of direct compression with wet and dry granulation [14]

Parameter	Direct compression	Wet granulation	Dry granulation
Granulation step	Not required	Required	Required
Drying step	Not required	Required	Not required
Processing time	Short	Long	Moderate
Energy requirement	Low	High	Moderate
Heat exposure	Low	Potentially high	Low–moderate
Moisture exposure	Low	High	Low
Equipment requirement	Lower	Higher	Moderate
Powder-flow requirement	High	Lower after granulation	Moderate
Manufacturing complexity	Low	High	Moderate

Microcrystalline Cellulose: Structure, Manufacture and Functionality

MCC is a purified, partially depolymerized cellulose material widely used as a pharmaceutical excipient. Cellulose consists of β-(1→4)-linked D-glucose units. MCC is generally produced by controlled hydrolysis of purified cellulose, preferentially modifying the less ordered regions and reducing the degree of polymerization. The resulting material retains crystalline domains and exhibits structural characteristics suitable for pharmaceutical applications [15].

MCC is commonly manufactured from cellulose-rich materials such as wood pulp and cotton. The general manufacturing process involves purification of the cellulose source, controlled acid hydrolysis, washing and neutralization, followed by drying and particle-size adjustment [16]. Differences in raw material source and manufacturing conditions can influence the physical characteristics and functional performance of the final material.

The functionality of MCC is not determined by chemical composition alone. Particle size, morphology, porosity, density, moisture content, crystallinity, degree of polymerization, and surface characteristics may influence powder flow, packing, deformation, and bonding behavior. Thus, different MCC grades may exhibit substantially different performance during direct compression. Commercial MCC variability has been associated with differences in attributes such as particle size, density, specific surface area, morphology, moisture content, degree of polymerization, and crystallinity [17].

Physicochemical and Functional Attributes of MCC [18,19]

1. Particle Size and Particle-Size Distribution

Particle size influences powder flow, packing, surface area, and compaction behavior. Smaller particles can provide greater specific surface area and potentially more interparticle contacts; however, very fine particles may exhibit increased cohesion and poorer flow. Larger particles may improve flow but can alter packing efficiency and bonding.

Particle-size distribution is also important because smaller particles can occupy void spaces between larger particles and thereby influence packing. Conversely, substantial size differences between MCC and other formulation components may increase segregation risk.

2. Particle Morphology

Particle morphology influences flow, packing, surface contact, and deformation. Differences in particle shape and surface structure can arise from

differences in raw material and manufacturing conditions. Morphology can consequently affect particle rearrangement during compression and the formation of interparticle contacts.

3. Porosity and Specific Surface Area

The porous structure of MCC contributes to its deformation and compaction behavior. Specific surface area influences the extent of contact between MCC particles and other formulation components. However, greater surface area can also increase interactions with moisture and lubricants.

4. Bulk and Tapped Density

Bulk and tapped density provide information regarding powder packing. Differences in density can influence blend homogeneity, die filling, and overall tablet weight. Tapped density has also been identified as a potentially important MCC material attribute associated with tabletability.

5. Moisture Content

Moisture content can influence the mechanical behavior and functionality of MCC. Water can act as a plasticizing agent and affect interparticle bonding, powder flow, and tablet strength. Therefore, moisture should be controlled during manufacturing and storage.

6. Crystallinity and Degree of Polymerization

MCC contains crystalline and less ordered regions. Its degree of crystallinity and degree of polymerization are associated with the structure of the cellulose material and may influence its mechanical behavior. Controlled depolymerization during manufacture contributes to the characteristic functionality of MCC.

7. Powder Flowability

Adequate flowability is essential for consistent die filling during direct compression. MCC is generally a useful direct-compression excipient, but its flow properties vary among grades. Particle size, morphology, density, moisture content, and surface characteristics contribute to this variability.

Table 2. Critical Material Attributes of MCC and Their Influence on Direct-Compression Performance

Critical Material Attribute	Influence On Powder Behavior	Potential Impact on Tablet Performance
Particle size and distribution	Flow, packing, segregation	Weight/content uniformity
Particle morphology	Flow, packing, contact area	Tabletability
Porosity and surface area	Densification, interparticle contact	Tablet strength
Bulk/tapped density	Packing and die filling	Weight variation
Moisture content	Plasticity, bonding	Strength and disintegration
Crystallinity	Deformation behavior	Compactibility
Degree of polymerization	Structural/mechanical behavior	Tabletability
Surface characteristics	Cohesion and lubrication	Bonding and tablet performance

Compressibility, Compactibility and Tabletability

Compressibility, compactibility, and tabletability describe related but distinct aspects of powder compaction and should not be used interchangeably.

Compressibility describes the ability of a powder bed to decrease in volume or increase in solid fraction under applied pressure.

Compactibility describes the ability of a powder to form a mechanically strong compact at a given degree of densification or solid fraction.

Tabletability describes the ability of a powder to produce a tablet of a specified mechanical strength at a given compaction pressure.

MCC is particularly valuable because of its favorable plastic deformation and bonding characteristics. Commercial-scale investigations have shown that multiple MCC material attributes can contribute to tabletability, rather than particle size or moisture alone.

Table 3. Compressibility, Compactibility and Tabletability of MCC

Property	Definition	Importance in MCC-based direct compression
Compressibility	Ability of powder to densify under pressure	Describes powder consolidation
Compactibility	Ability to form a strong compact at a given solid fraction	Indicates bonding efficiency
Tabletability	Ability to produce a strong tablet at a given pressure	Describes overall tableting performance

Mechanism of MCC During Compression

The excellent direct-compression performance of MCC is closely associated with its deformation and interparticle bonding behavior. Tablet formation involves particle rearrangement, deformation, densification, bonding, and elastic recovery.

During the initial stage of compression, MCC particles rearrange within the powder bed, reducing interparticle void spaces. With increasing pressure, MCC undergoes substantial plastic deformation. Plastic deformation increases the contact area between adjacent particles and promotes the formation of interparticle bonds. Continued compression produces further densification and formation of a coherent tablet matrix.

After removal of the compression force, partial elastic recovery occurs. Excessive elastic recovery may generate internal stresses and contribute to defects such as capping and lamination. Therefore, robust tablet formation depends on an appropriate balance between plastic deformation, bonding, densification, and elastic recovery [20,21].

The plastic deformation of MCC is a major reason for its high tabletability and dry-binding performance.

Compression Pathway:

MCC Material Attributes
↓
Particle Rearrangement
↓
Plastic Deformation
↓
Increased Interparticle Contact
↓
Interparticle Bonding
↓
Densification
↓
Tablet Formation
↓
Elastic Recovery
↓
Final Tablet Quality

MCC Grade and Source Variability

Commercial MCC is available in multiple grades differing in particle size, density, moisture content, morphology, and other functional characteristics. Therefore, grade selection should be based on formulation requirements rather than assuming equivalent performance among all MCC products [15,22].

Different grades can provide different balances between flowability and tabletability. Coarser materials may provide improved powder flow, whereas finer materials may provide different surface and bonding characteristics. The optimal grade therefore depends on API properties, formulation composition, required tablet characteristics, and manufacturing conditions.

Source-to-source and batch-to-batch variability may also influence MCC performance. Differences in cellulose source, hydrolysis, purification, drying, milling, and particle engineering can alter relevant material attributes [23]. These variations may subsequently influence flow, compaction, tablet strength, disintegration, and dissolution. Studies involving large numbers of commercially produced MCC samples demonstrate that attributes not always captured by conventional certificates of analysis can contribute to tabletability [24].

Table 4. Representative MCC Grades and General Functional Characteristics

MCC Grade	General Characteristic	Main Formulation Consideration
PH 101	Fine particle grade	Strong binding and compaction
PH 102	Coarser particle grade	Improved flow with good compaction
PH 103	Low-moisture grade	Moisture-sensitive formulations
PH 105	Very fine grade	High surface area/ bonding potential
PH 200	Coarser particle grade	Improved flow

Lubricant Sensitivity of MCC

Lubricants are essential in tablet manufacturing because they reduce friction between the powder blend and tablet-punch and die surfaces. Magnesium stearate is among the most widely used pharmaceutical lubricants. However, excessive lubricant concentration, intensive mixing, or prolonged lubrication can adversely affect the compaction behavior of plastically deforming materials such as MCC [25].

Lubrication can also influence disintegration and dissolution because hydrophobic lubricant films may reduce wetting and alter tablet structure [26,27]. Alternative lubricants have therefore been investigated to obtain adequate lubrication while minimizing negative effects on tablet strength and drug release.

MCC Based Co-Processed Excipients

Although MCC possesses excellent direct-compression functionality, limitations related to flowability, lubricant sensitivity, elastic recovery, and formulation-specific performance have encouraged the development of co-processed excipients. Co-processing combines two or more excipients through an engineered manufacturing process to obtain complementary functionality. MCC-based co-processed excipients can combine MCC's compactibility with improved flowability, disintegration, dilution potential, or other functions, providing multifunctional excipient platforms and potentially reducing formulation complexity [28,29,30].

Co-processing can modify particle size, morphology, porosity, surface characteristics, and powder packing, thereby influencing flow, compression, tabletability, disintegration, and dissolution. Research on biosourced MCC-containing co-processed systems has demonstrated that co-processing can simultaneously modify powder flow, tablet tensile

strength, compressibility, and disintegration, highlighting the potential of engineered MCC-based materials for direct compression [31,32].

Material To Performance Framework

The relationship between MCC material attributes and tablet quality can be represented as an integrated material-to-performance pathway.

MCC critical material attributes
Particle size | Morphology | Moisture | Density | Porosity | Crystallinity | Surface characteristics
↓
Powder functional properties
Flowability | Packing | Segregation tendency | Lubricant interaction
↓
Compression behavior
Compressibility | Compactibility | Plastic deformation | Interparticle bonding | Elastic recovery
↓
Tablet critical quality attributes
Weight | Tensile strength | Hardness | Friability | Disintegration | Dissolution | Content uniformity

This framework emphasizes that MCC material attributes should not be considered independently from formulation composition and process parameters. A change in one attribute may influence several downstream properties simultaneously. This material-to-performance approach is consistent with the broader emphasis in MCC literature on linking material attributes with final tablet performance.

API – MCC Interactions

The performance of microcrystalline cellulose (MCC) in direct compression is strongly influenced by its interactions with the API and other formulation components. API properties such as particle size, morphology, density, surface characteristics, dose fraction, compactibility, and flow behavior can alter blend characteristics and determine the functional contribution of MCC during tablet formation. The relative proportions of API and MCC are important because MCC concentration affects powder flow, compaction, interparticle bonding, and tablet strength. High-dose APIs may reduce the MCC available for binding, whereas poorly compactible APIs may increase dependence on MCC to achieve adequate tablet strength [33,34].

Differences in particle size, density, morphology, and surface characteristics between the API and MCC can influence mixing, packing, and segregation. Fine, cohesive APIs may exhibit poor flow and form agglomerates, whereas larger or denser particles may segregate from the MCC-rich fraction during blending, transfer, and die filling. Such differences can affect API distribution, content uniformity, and tablet consistency [35,36,37]. Surface interactions between API and MCC may further influence interparticle adhesion, deformation, bonding, tablet structure, disintegration, and dissolution.

Therefore, MCC should not be selected solely on the basis of its intrinsic compactibility or flow properties. Effective formulation development should consider API characteristics together with MCC grade, concentration, particle-size distribution, lubricant level, blending conditions, and compression parameters. Systematic evaluation of these factors can support appropriate MCC selection and improve the robustness and consistency of direct-compression formulations.

Influence of MCC on Tablet Critical Quality Attributes

The influence of MCC extends from powder flow and compaction to the critical quality attributes

(CQAs) of the finished tablet. However, these CQAs are determined by the combined effects of MCC material attributes, API properties, formulation composition, and process parameters [38,39]. Tablet tensile strength is influenced by deformation and interparticle bonding. Appropriate MCC selection and compression conditions can contribute to mechanically robust tablets with low friability, whereas excessive elastic recovery or inappropriate compression conditions may increase the risk of capping and lamination. MCC grade, particle size, moisture content, density, and porosity can further influence powder packing and compaction behavior.

Disintegration and dissolution are influenced by MCC concentration, tablet porosity, compression force, drug properties, and other excipients. Increased tablet strength does not necessarily result in improved disintegration or dissolution, as higher compression forces may reduce porosity and restrict liquid penetration. Weight and content uniformity depend on powder flow, particle-size distribution, density differences, segregation tendency, blending, and die filling. Therefore, MCC should be evaluated as part of the complete formulation, considering material attributes, formulation variables, and process conditions to achieve consistent tablet quality and robust manufacturing performance [40].

Research Gaps and Future Perspectives

Despite the extensive use of microcrystalline cellulose (MCC) in pharmaceutical manufacturing, several research gaps remain. A deeper understanding of the relationships between MCC material attributes and tablet performance is needed across different grades, suppliers, and manufacturing processes. Although particle size, moisture content, density, porosity, and morphology influence tabletability, their relative effects may vary with formulation and processing conditions. Standardized functional characterization of MCC, including powder flow, deformation, compaction, and tabletability, could support rational grade selection and improve formulation consistency. Lubricant sensitivity also warrants further investigation because interactions among MCC, lubricant type and concentration, blending conditions, and compression parameters can significantly affect tabletability and mechanical strength.

MCC-based co-processed excipients represent an important area for future development. Rational particle engineering should establish relationships between processing conditions, particle structure, material attributes, deformation behavior, and tablet performance rather than relying primarily on empirical screening. Furthermore, the increasing adoption of continuous manufacturing requires consistent powder flow, feeding behavior, and material performance, highlighting the need for improved functional characterization and real-time monitoring of MCC-containing formulations.

Mechanistic modeling, multivariate analysis, machine learning, and artificial intelligence offer promising approaches for predicting relationships among material attributes, formulation composition, process parameters, and tablet quality. Integration of these tools with advanced experimental characterization could improve excipient selection, reduce formulation-development effort, and support robust and predictable direct-compression manufacturing. Future research should therefore integrate material science, advanced characterization, process monitoring, and predictive modeling to optimize MCC functionality and expand its applications in modern tablet manufacturing.

Table 5. Current Challenges and Future Opportunities for MCC in Direct Compression

Current Challenge	Effect on Formulation	Future Opportunity
MCC grade/ source variability	Variable functionality	Advanced material characterization
Lubricant sensitivity	Reduced tabletability	Optimized lubrication strategies
API–MCC interaction	Variable flow and compaction	Predictive compatibility assessment
Co-processed excipients	Complex structure–function relationships	Rational excipient engineering
Continuous manufacturing	Need for consistent powder behavior	Real-time material monitoring
Limited predictive models	Empirical formulation development	Mechanistic and data-driven models

CONCLUSION

Microcrystalline cellulose (MCC) remains an important pharmaceutical excipient for direct-compression tableting because of its excellent compactibility, tabletability, dry-binding capacity, and plastic deformation behavior. Its performance is influenced by material attributes such as particle size, morphology, density, porosity, moisture content, crystallinity, surface characteristics, grade, and manufacturing conditions. Therefore, rational MCC selection should consider both compendial quality and functional material attributes. Understanding the relationships among MCC properties, powder behavior, deformation, compression, lubrication, and tablet quality is essential for developing robust direct-compression formulations. MCC-based co-processed excipients offer opportunities to improve powder flow, compaction, and formulation versatility. Advanced material characterization and predictive approaches may further improve understanding of structure–function relationships and support more reliable excipient selection. Continuous manufacturing and data-driven formulation development also represent promising future directions. Overall, adopting a material-to-performance approach can enhance formulation robustness, manufacturing consistency, and pharmaceutical development and innovation, supporting the effective application of MCC in modern direct-compression tablet manufacturing across diverse pharmaceutical formulation and manufacturing requirements in modern practice.

REFERENCES

1. Chen H, Aburub A, Sun CC. Direct compression tablet containing 99% active ingredient—a tale of spherical crystallization. Journal of pharmaceutical sciences. 2019 Apr 1;108(4):1396-400.
2. Aulton ME, Taylor K, editors. Aulton's pharmaceutics: the design and manufacture of medicines. Elsevier Health Sciences; 2013.
3. Zhao H, Zhao L, Lin X, Shen L. An update on microcrystalline cellulose in direct compression: Functionality, critical material attributes, and co-processed excipients. Carbohydrate polymers. 2022 Feb 15;278:118968.
4. Thoorens G, Krier F, Rozet E, Carlin B, Evrard B. Understanding the impact of microcrystalline cellulose physicochemical properties on tabletability. International journal of pharmaceutics. 2015 Jul 25;490(1-2):47-54.
5. Thoorens G, Krier F, Leclercq B, Carlin B, Evrard B. Microcrystalline cellulose, a direct compression binder in a quality by design environment—A review. International journal of pharmaceutics. 2014 Oct 1;473(1-2):64-72.
6. Sun CC. Mechanism of moisture induced variations in true density and compaction properties of microcrystalline cellulose. International journal of pharmaceutics. 2008 Jan 4;346(1-2):93-101.
7. Azad MA, Capellades G, Wang AB, Klee DM, Hammersmith G, Rapp K, Brancazio D,

Myerson AS. Impact of critical material attributes (CMAs)-particle shape on miniature pharmaceutical unit operations. Aaps Pharmscitech. 2021 Mar 11;22(3):98.
8. Zhao H, Shi C, Zhao L, Wang Y, Shen L. Influences of different microcrystalline cellulose (MCC) grades on tablet quality and compression behavior of MCC-lactose binary mixtures. Journal of Drug Delivery Science and Technology. 2022 Nov 1;77:103893.
9. Bolhuis GK, Anthony Armstrong N. Excipients for direct compaction—an update. Pharmaceutical development and technology. 2006 Jan 1;11(1):111-24.
10. Armstrong NA. Tablet manufacture by direct compression. InEncyclopedia of Pharmaceutical Science and Technology, Six Volume Set (Print) 2013 Jul 1 (pp. 3539-3549). CRC Press.
11. Van Snick B, Holman J, Vanhoorne V, Kumar A, De Beer T, Remon JP, Vervaet C. Development of a continuous direct compression platform for low-dose drug products. International journal of pharmaceutics. 2017 Aug 30;529(1-2):329-46.
12. Jivraj M, Martini LG, Thomson CM. An overview of the different excipients useful for the direct compression of tablets. Pharmaceutical science & technology today. 2000 Feb 1;3(2):58-63.
13. Carlin BA. Direct Compression and the Role. Pharmaceutical Dosage Forms-Tablets: Rational Design and Formulation. 2008 Jun 3;2:173.
14. Šantl M, Ilić I, Vrečer F, Baumgartner S. A compressibility and compactibility study of real tableting mixtures: The impact of wet and dry granulation versus a direct tableting mixture. International journal of pharmaceutics. 2011 Jul 29;414(1-2):131-9.
15. Chaerunisaa AY, Sriwidodo S, Abdassah M. Microcrystalline cellulose as pharmaceutical excipient. Pharmaceutical formulation design-recent practices. 2019 Jul 19:1-21.
16. El-Sakhawy M, Hassan ML. Physical and mechanical properties of microcrystalline cellulose prepared from agricultural residues. Carbohydrate polymers. 2007 Jan 2;67(1):1-0.
17. Trache D, Hussin MH, Haafiz MM, Thakur VK. Recent progress in cellulose nanocrystals: sources and production. Nanoscale. 2017 Feb 2;9(5):1763-86.
18. Kalita P, Roy PK, Das N, Pachuau L. Silicified microcrystalline cellulose from renewable banana pseudostem: Physicochemical and functional analysis. International Journal of Biological Macromolecules. 2024 Dec 1;283:137620.
19. Zhong F, Nsor-Atindana J. Microcrystalline cellulose and nanocrystalline cellulose. InHandbook of Hydrocolloids 2021 Jan 1 (pp. 509-536). Woodhead Publishing.
20. Paul S, Sun CC. Gaining insight into tablet capping tendency from compaction simulation. International journal of pharmaceutics. 2017 May 30;524(1-2):111-20.
21. Dwivedi SK, Oates RJ, Mitchell AG. Estimation of elastic recovery, work of decompression and Young's modulus using a rotary tablet press. Journal of pharmacy and pharmacology. 1992 Jun;44(6):459-66.
22. Doelker E. Comparative compaction properties of various microcrystalline cellulose types and generic products. Drug development and industrial pharmacy. 1993 Jan 1;19(17-18):2399-471.
23. Portier C, Vigh T, Di Pretoro G, Leys J, Klingeleers D, De Beer T, Vervaet C, Vanhoorne V. Continuous twin screw granulation: Impact of microcrystalline cellulose batch-to-batch variability during granulation and drying–A QbD approach. International journal of pharmaceutics: X. 2021 Dec 1;3:100077.
24. Fonteyne M, Correia A, De Plecker S, Vercruysse J, Ilić I, Zhou Q, Vervaet C, Remon JP, Onofre F, Bulone V, De Beer T. Impact of microcrystalline cellulose material attributes: A case study on continuous twin screw granulation. International journal of pharmaceutics. 2015 Jan 30;478(2):705-17.
25. Dun J, Chen H, Sun CC. Profound tabletability deterioration of microcrystalline

cellulose by magnesium stearate. International journal of pharmaceutics. 2020 Nov 30;590:119927.
26. Zuurman K, Van der Voort Maarschalk K, Bolhuis GK. Effect of magnesium stearate on bonding and porosity expansion of tablets produced from materials with different consolidation properties. International journal of pharmaceutics. 1999 Mar 1;179(1):107-15.
27. de Backere C, Quodbach J, De Beer T, Vervaet C, Vanhoorne V. Impact of alternative lubricants on process and tablet quality for direct compression. International Journal of Pharmaceutics. 2022 Aug 25;624:122012.
28. Benabbas R, Sanchez-Ballester NM, Bataille B, Sharkawi T, Soulairol I. Development and pharmaceutical performance of a novel co-processed excipient of alginic acid and microcrystalline cellulose. Powder technology. 2021 Jan 22;378:576-84.
29. Dai X, Wang J, Yan B, Wang Q, Shen Y, Chen Y, Tian Y. A novel lactose/MCC/L-HPC triple-based co-processed excipients with improved tableting performance designed for metoclopramide orally disintegrating tablets. Pharmaceutics. 2024 Jul 19;16(7):959.
30. Goyanes A, Martínez-Pacheco R. New co-processed MCC-based excipient for fast release of low solubility drugs from pellets prepared by extrusion-spheronization. Drug development and industrial pharmacy. 2015 Mar 4;41(3):362-8.
31. Medarević D, Čežek M, Djuriš M, Marković B, Djuriš J, Maksimović Z. Development of co-processed excipient from wheat harvest residue-derived microcrystalline cellulose suitable for formulation of immediate release tablets containing high-dose drug. Cellulose. 2025 Sep;32(13):7783-802.
32. Rojas J, Buckner I, Kumar V. Co-proccessed excipients with enhanced direct compression functionality for improved tableting performance. Drug development and industrial pharmacy. 2012 Oct 1;38(10):1159-70.
33. Bharate SS, Bharate SB, Bajaj AN. Interactions and incompatibilities of pharmaceutical excipients with active pharmaceutical ingredients: a comprehensive review. International Journal of Pharmaceutical Excipients. 2016 Nov 23;1(3).
34. Ridgway C, Bawuah P, Markl D, Zeitler JA, Ketolainen J, Peiponen KE, Gane P. On the role of API in determining porosity, pore structure and bulk modulus of the skeletal material in pharmaceutical tablets formed with MCC as sole excipient. International journal of pharmaceutics. 2017 Jun 30;526(1-2):321-31.
35. Sinka IC, Motazedian F, Cocks AC, Pitt KG. The effect of processing parameters on pharmaceutical tablet properties. Powder Technology. 2009 Jan 31;189(2):276-84.
36. Zakhvatayeva A, Zhong W, Makroo HA, Hare C, Wu CY. An experimental study of die filling of pharmaceutical powders using a rotary die filling system. International Journal of Pharmaceutics. 2018 Dec 20;553(1-2):84-96.
37. Sun CC. Setting the bar for powder flow properties in successful high speed tableting. Powder technology. 2010 Jul 12;201(1):106-8.
38. Yu LX, Amidon G, Khan MA, Hoag SW, Polli J, Raju GK, Woodcock J. Understanding pharmaceutical quality by design. The AAPS journal. 2014 Jul;16(4):771-83.
39. Yu LX. Pharmaceutical quality by design: product and process development, understanding, and control. Pharmaceutical research. 2008 Apr;25(4):781-91.
40. Maclean N, Walsh E, Soundaranathan M, Khadra I, Mann J, Williams H, Markl D. Exploring the performance-controlling tablet disintegration mechanisms for direct compression formulations. International journal of pharmaceutics. 2021 Apr 15;599:120221.
41. Haafiz MM, Eichhorn SJ, Hassan A, Jawaid M. Isolation and characterization of microcrystalline cellulose from oil palm

biomass residue. Carbohydrate polymers. 2013 Apr 2;93(2):628-34.
42. Landin M, Martínez-Pacheco R, Gómez-Amoza JL, Souto C, Concheiro A, Rowe RC. Influence of microcrystalline cellulose source and batch variation on the tabletting behaviour and stability of prednisone formulations. International journal of pharmaceutics. 1993 Apr 26;91(2-3):143-9.
43. Williams RO, Sriwongjanya M, Barron MK. Compaction properties of microcrystalline cellulose using tableting indices. Drug development and industrial pharmacy. 1997 Jan 1;23(7):695-704.
44. Amidon GE, Houghton ME. The effect of moisture on the mechanical and powder flow properties of microcrystalline cellulose. Pharmaceutical research. 1995 Jun;12(6):923-9.
45. Al-Dulaimi AA, Wanrosli WD. Isolation and characterization of nanocrystalline cellulose from totally chlorine free oil palm empty fruit bunch pulp. Journal of Polymers and the Environment. 2017 Jun;25(2):192-202.

HOW TO CITE: Harshwardhan Lohar, Avantika Mane, Vinayak Patil, Jayant Patil, Microcrystalline Cellulose in Direct Compression: Material Attributes, Compaction Behavior, and Tablet Performance, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 8, 4442-4455. https://doi.org/10.5281/zenodo.22120642