Elucidating Compaction Properties of Different Mannitol and Lactose Grades by Compaction Simulation
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Purpose
Mannitol and lactose are commonly used excipients in pharmaceutical tablets. Different grades of both mannitol and lactose are commercially available. They exhibit significant variations in particulate and powder properties that can impact tablet manufacturability. Choice of sub-optimum type or grade of excipient in tablet formulation can lead to manufacturing problems and difficulties, which is magnified when the manufacturing process is continuous. Hence, this research work seeks to comprehensively characterize the compaction properties of different mannitol and lactose grades by using two types of modern compaction simulators. Such information will facilitate the choice of the most suitable type and grade of excipient when developing a tablet product.

Methods
Eleven mannitol and five lactose grades of powder were studied. These include milled crystalline (MC) lactose (110M and 350M) or mannitol (25C, 50C and 160C), spray-dried (SD) lactose (11SD) or mannitol (100SD and 200SD), granulated lactose (GC) (24AN, 30GR) or mannitol (300DC, 400DC and 500DC) and crystalline processed (PC) mannitol (M100, M200 and M300). Powders were compacted on Presster at tableting speeds 10 ms and 100 ms and tablets were diametrically broken on a texture analyzer to determine tensile strength. Tablet brittleness index (TBI) was obtained from the tablet breaking force data. Powder compressibility data was analyzed using Kuentz-Leuenberger equation. Die-wall stress data was obtained using an instrumented die. Strain rate sensitivity of the powders was also assessed based on the data at the two speeds. These powders were also studied using a hydraulic compaction simulator (ESH Testing Limited, 2000, UK), where in die data was collected and analyzed to obtain mean yield pressure at two different speeds, and subsequently strain rate sensitivity (SRS) of different powders were determined.

Results
Tabletability of different mannitol grades followed PC > SD > MC > GC at both speeds. The lactose grades followed the order SD ≥ GC > MC. The compactibility profiles were also same, implying the critical role of bonding strengths on the tabletability of these powders. The intrinsic bonding strength (σ₀) correlated positively and linearly with the BET surface area but correlated negatively with KL plasticity parameter, 1/C, implying the significant roles of bonding area on powder tabletability. TBI correlated negatively with σ₀, indicating weaker tablets were more brittle. More plastic materials (lower 1/C) also showed stress transmission closer to unity. At a solid fraction of 0.85, adequate tensile strength (1.5-2.0 MPa) was attained by PC and SD (mannitol) and GC (lactose) grades only. Both plasticity (1/C) and TBI₀ followed the order PC > SD > GC > MC for both mannitol and lactose. The SRS data from hydraulic compaction simulator suggests that PC grades of mannitol were least susceptible (SRS = 2.0%) compared to MC and GC grades (SRS = 18 – 25%) to change in tableting speed. In case of 5 lactose grades, SRS was low (SRS <5.6%), indicating little effect of tablet speed on their compression behavior.

Conclusion
The study showed significant variations in compaction properties of the 16 grades of mannitol and lactose. PC and SD grades exhibited better tabletability and, therefore, provide improved mechanical strength to the formulation. These grades were also found more plastic and less brittle than MC and GC grades of mannitol and MC grade of lactose. This study has documented important mechanical properties of commonly available mannitol and lactose grades. Such knowledge is valuable for guiding the selection of suitable excipient to attain high quality tablet products.