Surface area of lactose and lactose granulates on consolidation and compaction

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Chapter 11

Summary

Tablets are the most widely used oral pharmaceutical dosage forms. They are produced by compression of powder mixtures, which contain, next to the active principle, several ingredients, necessary to obtain a compact with the required properties. One of the components used in tablets is the filler-binder lactose. Previous studies on the consolidation and compaction properties of narrow sieve fractions of (crystalline) lactose revealed that the bonding strength of lactose tablets depends on the type of lactose used, the particle size fraction and the compaction load. It was demonstrated that lactose mainly fragments during tabletting, resulting in an increase in the specific surface area. For tablets compacted from homogeneous systems of single sieve fractions of crystalline lactose a unique direct relationship was demonstrated between strength and specific surface area. However, strength and specific surface area were measured on tablets stored for different time periods under different storage conditions. This dissertation discusses the effect of short time storage at different conditions on the strength and the specific BET-surface area of lactose tablets. In addition, some aspects are studied of the consolidation and compaction properties of crystalline lactose fractions in heterogeneous systems. The crystalline lactose types used are: α-lactose monohydrate, anhydrous α-lactose, crystalline β-lactose and roller dried β-lactose.

In chapter 2 the effect of storage conditions on the strength and the specific BET-surface area of lactose tablets are discussed. It is demonstrated that tablets compacted from α-lactose monohydrate and from roller dried β-lactose both show time-dependent moisture uptake when exposed to an ambient humid atmosphere. Moisture sorption tends to reach a plateau within 10 min and is accompanied with a decrease in both crushing strength and specific BET-surface area of the tablets. Subsequent storage of the tablets in a dry atmosphere results in an increase in strength but no change in surface area. The tablets show no moisture uptake, nor any change in strength and surface area when transferred immediately after ejection from the die into a dry atmosphere. These results are indicative for dissolution of contact points between lactose particles in a tablet when exposed to a humid atmosphere and recrystallization of dissolved lactose when transferred from a humid into a dry atmosphere. The irreversible decrease in specific surface area of the tablets on exposure to humid conditions is suggested to be caused by blocking of the very narrow pores in the tablets by sorbed moisture. These changes in crushing strength endorse the need to standardize the time between tablet ejection and strength measurement. Concerning the BET-specific surface area, it is recommended to suppress blocking of small pores by transferring the tablets immediately after ejection from the die into a dry nitrogen atmosphere for transport to the gas adsorption apparatus.

The effect of water sorption on the specific tablet surface area is further examined in chapter 3. The study described in this chapter has been performed to proof the general significance

of moisture sorption in tablets by extending the surface area determinations to excipients with different water solubilities. It is demonstrated that tablets compacted from both water soluble and water insoluble particulate solids show no change in BET-specific surface area when transferred immediately after ejection from the die into a dry atmosphere. Storage at ambient humidity results into an irreversible decrease in surface area, caused by capillary condensation of moisture and blocking of pores in the tablet. This conclusion is supported by nitrogen fysisorption isotherms performed on crystalline β-lactose tablets. Uptake of water in the mesopores diminishes the accessible surface in the tablets. Removement of adsorbed water results into a small increase of the BET-surface area only.

Chapter 4 is the first chapter in which the consolidation and compaction properties of powder mixtures of crystalline lactose are discussed. Binary mixtures of four different types of crystalline lactose: α-lactose monohydrate, anhydrous α-lactose, roller-dried β-lactose and crystalline β-lactose, were compressed into tablets. The results show a proportional intercorrelation of the crushing strength and internal specific surface area of the tablets, respectively, with the composition of the powder blend, when compressed from binary mixtures of same particle size fraction. All data are found to fit the unique relationship between the crushing strength and the internal specific surface area of crystalline lactose tablets. It is concluded that binary mixtures of same particle size fractions of different types of crystalline lactose exhibit no interaction between the components during consolidation.

Chapter 5 deals with the consolidation and compaction properties of binary mixtures of different particle size fractions of α-lactose monohydrate. The results show decreased crushing strengths and decreased internal specific surface areas of the tablets as compared with the values calculated by linear interpolation of the data obtained for the corresponding single powder fractions. The extent of decreased strength and decreased surface area of the tablets is found to depend upon the weight ratio of the finer sieve fraction in the blend and to increase with the diameter ratio between coarse and finer particles. These results indicate an interaction with respect to consolidation and compaction and is explained by decreased fragmentation potentials, caused by increased packing densities of the binary mixtures of different particle size fractions of crystalline lactose. All data of crushing strength and internal specific surface area of the tablets fit the unique linear relationship between these parameters, as found previously for tablets compressed from binary mixtures of equal particle size fractions of different types of crystalline lactose.

Chapter 6 is the last chapter discussing the consolidation and compaction properties of powder mixtures of crystalline lactose. Tablets were compacted from a coarse fraction (250–315 μm), a fine fraction (32–45 μm) and from binary blends of a coarse and a fine fraction of different types of crystalline lactose. The results show differences in consolidation and compaction between the granular lactose types, i.e. roller dried β-lactose and anhydrous α-lactose, and non-granular lactose types, namely crystalline β-lactose and α-lactose monohydrate. Particles of the granular types of lactose exhibit greater specific powder surface areas, less fragmentation on compression, and higher binding capacities than the particles of the non-granular types. Slight increases in consolidation are demonstrated on compression of binary blends of the coarse and the fine fraction of the different types of lactose. Differences in morphology between the lactose types are shown by increasing true densities of the granular types when examined on tablets compacted with increasing compression force. No change in true densities on compaction are demonstrated by the non-granular types.

In chapter 7 a new explanation of the effect of magnesium stearate on tablet strength is proposed. This paper reports that magnesium stearate sensitivity of brittle materials is not directly related to the degree of fragmentation during compression. A coherent matrix of magnesium stearate, created by the process of dry blending, is highly sustained during consolidation and

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compaction of the particulate system. Failure of the tablets happens therefore principally along the interfaces of the original excipient crystals. Fragmentation of the excipient particles occurs mainly within the areas surrounded by the magnesium stearate network and contributes therefore little to the crushing strength of the tablets.

Chapter 8 is the first of the two chapters dealing with the relationship between properties of granulations prepared from crystalline lactose on the one hand and tabletting properties on the other. The consolidation and compaction properties of granule fractions prepared by dry granulation (slugging) of α-lactose monohydrate and roller-dried β-lactose, respectively, are studied. The results show that the compactibility of the granule fractions is determined by the type of lactose used and the granule size. The tablets compacted from the granule fractions show almost equal crushing strength but a higher specific BET-surface area as compared with the surface area of the slugs. Influence of granule size on tablet strength points to a relation between outside surface area of granules and tablet strength. Obviously granule particles sustain their integrity to some extent during compaction. Air permeability and mercury porosimetry show that in tablets with equal strength different pore systems can exist. Generally, tablets compacted from fine granule size fractions exhibit finer pore sizes and higher strengths compared to the tablets compacted from coarse size fractions. Furthermore, mercury porosimetry reveals that the whole pore system determines tablet strength. This means that granule particles deform during consolidation. The influence of the starting materials on tablet strength cannot be explained by permeametry surface area measurements and mercury porosimetry. It is suggested that differences in the internal structure between the granules of the two lactose types are responsible.

Chapter 9 evaluates the relationship between the bulk density and the compactibility of crystalline lactose. Granulations were prepared from α-lactose monohydrate and roller dried β-lactose powders by wet granulation, using different techniques with only water as a binder, or by slugging. The results demonstrate that by the process of granulation of one lactose powder, granules with different bulk densities and different compactibilities can be prepared. In addition to the type of lactose used, the compactibility of the granule fractions is dependent on the bulk density of the granule fraction. Generally, with an increase in the bulk density, the compactibility of a granule fraction decreases. Little variation is observed between the inter-granular porosities of the granule fractions. More differences are found between the intra-granular porosities of the granule fractions. However, the compactibility of granule fractions of one lactose type is mainly determined by the total porosity of the granule powder bed. Mercury porosimetry determinations on tablets compacted from the granule fractions show a relationship between the tablet pore system and compact strength: compression of granulations with a high bulk density results into tablets with a high average pore radius and a low crushing strength. Obviously, the possibility to deform a granule fraction during compression, the deformation potential, is determined by the total porosity of the powder bed. A high deformation potential, i.e. a high compactibility, can be obtained by using a granulation procedure in which granulations with a low bulk density are produced.