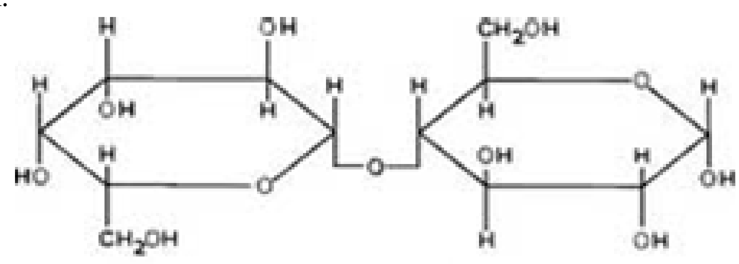
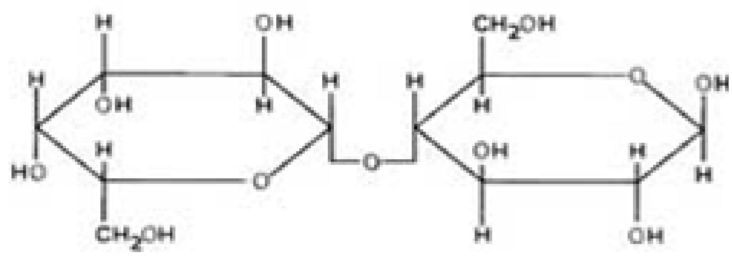
Lactose

Although it is probably the oldest excipient used in solid dosage form formulations, lactose is still one of the most widely used excipients in the pharmaceutical industry. Lactose is usually used as a filler and diluent in tablets and capsules, and to a more limited extent in lyophilized products and infant formulas. Lactose is also used as a diluent in dry-powder inhalation. Lactose occurs as white to off-white crystalline particles or powder. It is odorless and slightly sweet-tasting.

The lactoses used as pharmaceutical excipients belong to a group of compounds based upon the natural disaccharides of galactose and glucose produced from cow's milk, which contains about 4.6% lactose, corresponding to about 38% of its dry solids. Lactose has two anomers (stereo-isomers), α and β, differing only in the configuration of the hydroxyl group at the anomeric hemiacetal carbon. α has an axial hydroxyl whereas β hydroxyl is equatorial (Figure 1). [1-3] The β-isomer is obtained by crystallization above 93.5° C as a non-hygroscopic anhydrous form.



α-lactose



β-lactose

Figure 1: Structure of α- and β-lactose types

The α-isomer, obtained by crystallization at lower temperatures, forms a monohydrate, which can be dehydrated to yield a stable (non-hygroscopic) anhydrous form above 130°C or an unstable (hygroscopic) form at lower temperatures.[3] Spray dried lactose has been introduced in 1958[1] and it is one of the oldest directly compressible fillers available in the market.

Anhydrous lactose is widely used in direct compression tableting applications, and as a tablet and capsule filler and binder. It may also be used in intravenous injections. Anhydrous lactose occurs as white to off-white crystalline particles or powder. It is typically anhydrous β-lactose (O-β-d-galactopyranosyl-(1→4)-β-d-glucopyranose) and anhydrous α-lactose; or a mixture of O-β-d-galactopyranosyl-(1→4)-α-d-glucopyranose and O-β-d-galactopyranosyl-(1→4)-β-d-glucopyranose. (USP32–NF27)

It may be modified as to its physical characteristics, and may contain varying proportions of amorphous lactose. (USP32–NF27) Its systematic name of alpha lactose monohydrate is β-D-galactopyranosyl-(1→4) -α-D-glucopyranose. Various lactose grades are commercially available that have different physical properties such as particle size distribution and flow characteristics. The family of lactose products is shown in Figure 2.

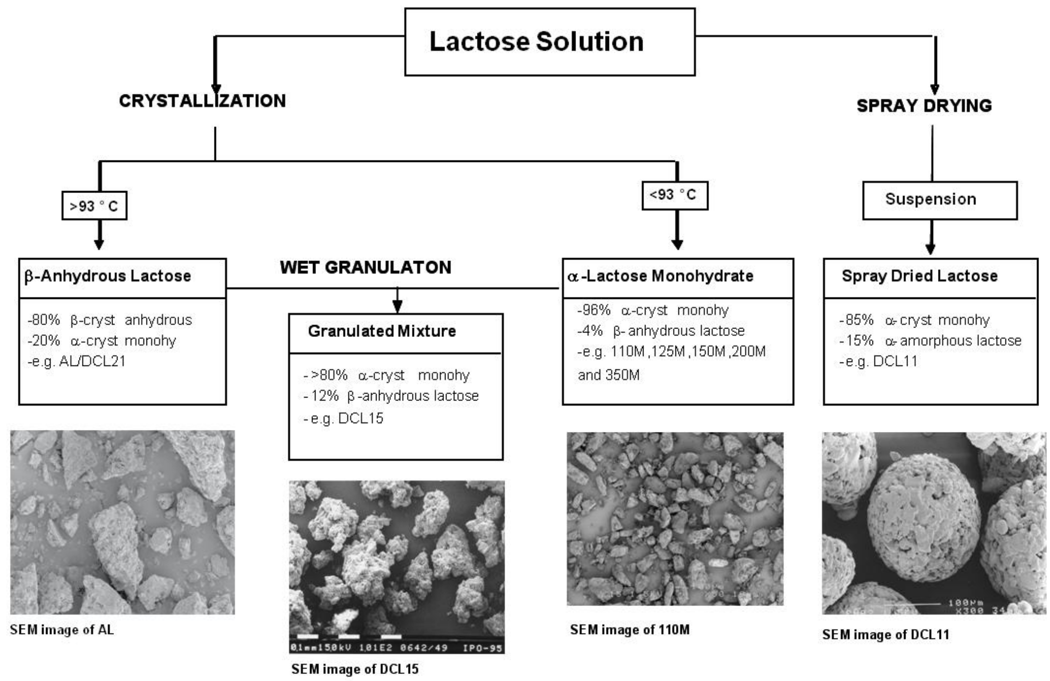


Figure 2: Schematic showing variation in the manufacturing process different types of lactose and their SEM pictures (as provided by vendor)

Vromans et al.[4,5] studied the consolidation and compaction behavior of α-lactose monohydrate (95% pure) and spray dried anhydrous lactose (having 80% α-lactose monohydrate) in tableting. Mercury porosimetry was used to demonstrate that crystalline lactose fragments during compaction. Tablet strength was found to be dependent on the degree of fragmentation only. This finding indicated that the nature of actual binding must be the same for different types of crystalline lactose. Later Boer et al.[6] while working on different sieve fraction of α-lactose monohydrate (95% pure) found that under consolidated load fine particles undergo more fragmentation that leads to increase in specific surface area thus forming higher binding surfaces leading to higher tensile strength of tablets. It was also demonstrated that neither the α/β ratio nor the amount of water of crystallization influences the binding mechanism. Lerk et al. reported that α-lactose monohydrate is a poor binder whereas anhydrous lactose (mainly β-anhydrous lactose) is a superior binder but has borderline flowability.[7]

Whiteman and Yarwood worked on six different types of lactose, they are: 1. Fast-Flo Lactose (spray-dried α-lactose monohydrate from vendor K & K Greeff Ltd), 2. Lactose NF (α-lactose monohydrate), 3. Anhydrous lactose (85% β-anhydrous lactose), 4. Tablettose (physically modified α-lactose monohydrate), 5. Zeparox (spray-dried α-lactose monohydrate from vendor Dairy Crest Ltd), 6. Ludipress (α-lactose monohydrate + 2.2% PVP+3.4% crospovidone). They found that anhydrous lactose possessed superior compactibiltiy and gave the strongest tablets, followed by Ludipress and Fast Flo.

Tablettose produced much weaker tablets. It had been reported in previous tableting studies that spray-dried lactose possessed excellent compactibility, only second to anhydrous lactose.[8,9] Tattawasart et al while working on the application of α-lactose monohydrate studied lubricant concentration, compression pressure and tamping pin height on plug height, plug porosity, plug weight variation and ejection forces.[10] It was found that plug porosity, both under compression and after ejection, was found to be dependent on dosator pressure. Plug weight and length were dependent on dosator piston height and uniformity of plug weight was independent of all the factors studied. Plug ejection pressure was dependent on dosator piston height, even when ejection pressure was corrected for changes in plug length.

References

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