

## Control of Size and Morphology of $\alpha$ -Lactose Monohydrate Crystals by using Structurally Related Additives -Possible Consequences for Dehydration Behaviour and Amorphisation.

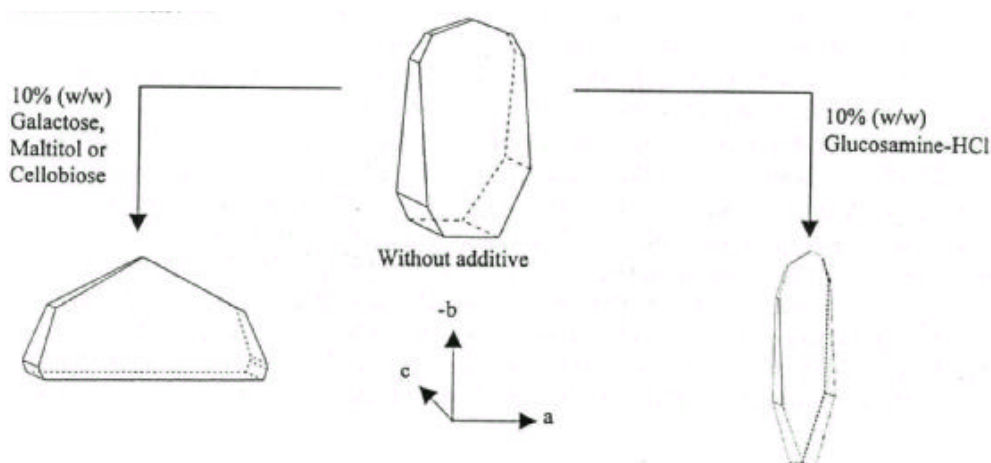
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Since  $\alpha$ -lactose is one of the most common excipients (associated with about 2500 drugs), the knowledge of its crystallisation mechanism and the control of its crystal morphology can have important consequences in terms of amorphisation and dehydration feasibility.'

Although some investigations have already been devoted to the influence of structurally related additives on the morphology of  $\alpha$ -L-H<sub>2</sub>O single crystals,<sup>2</sup> neither a systematic study nor a structural explanation have been reported up to now.

The present work shows that two types of morphological changes can be depicted when crystals are grown in aqueous medium at room temperature with various proportions of mono- or disaccharides additives:



These experimental results can be explained on the basis of structural data,<sup>3</sup> by studying the possible adsorption facility and/or desorption difficulty of the additives on the major crystal surfaces. More precisely, the ability of the adsorbed additives to maintain the H-bond network for specific faces can result in a significant decrease of the growth rate along this direction.<sup>5</sup>

The morphological changes induced by selected additives are likely to modify the amorphisation behaviour induced by lyophilisation or grinding, as well as the dehydration behaviour. Indeed, in the course of dehydration of  $\alpha$ -L-H<sub>2</sub>O crystals, water molecules are probably evacuated along channels parallel to the c-axis<sup>1</sup>. Therefore, a drastic change in the thickness along c can significantly modify the rate and the mechanism of dehydration, due for instance to lower amounts of associated microstrains.

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