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**Development of a continuous process to produce  
the 1:1  $\beta/\alpha$  mixed lactose crystal**

A thesis in partial fulfilment of the requirements for the degree of  
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University

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## ABSTRACT

A new lactose crystal was formed at Massey University in 1997 while studying the effects of superheated steam on the production of  $\beta$ -lactose. The crystal typically had 50-52%  $\beta$ -lactose content and an X-ray diffraction pattern that did not match with either  $\beta$ -lactose or  $\alpha$ -lactose monohydrate, and so it was thought to be an entirely new lactose crystal. Preliminary work was then done at Massey University to determine the conditions under which the crystal could be produced. The new crystal was produced in a batch process in a superheated steam environment between the temperatures of 125°C to 155°C and at very fast drying rates.

The present work attempts to develop a continuous process to produce this new lactose crystal. During the late stages of the project it was found that a similar crystal was already documented in the literature and its crystal structure defined. So the crystal found at Massey University could not be termed as a new crystal. The crystal found in the literature was formed by a high thermal treatment to solid-state  $\alpha$ -lactose monohydrate and amorphous lactose and had a  $\beta/\alpha$  anomeric ratio of 1:1. The present work attempts to develop a continuous process to produce the 1:1  $\beta/\alpha$  mixed lactose crystal from a liquid state and in a superheated steam environment.

A roller drier was thought to be the best option to produce the new crystal in a continuous process. Different arrangements were developed to create the required conditions under which it was expected that the 1:1  $\beta/\alpha$  mixed lactose crystal would be produced. Lactose solution sprayed on the roller drier using spray nozzles at temperatures of 125°C to 155°C and flow rates in the range of 110ml/min to 40ml/min with varying drum speeds consistently produced 85%  $\beta$ -lactose. Lactose solution was smeared on the drum surface which also produced about 80%  $\beta$ -lactose. Lactose solution that was sprayed over a tray which was designed to allow only small amount of the solution (about 3ml/min) to pass through produced about 58%  $\beta$ -lactose. X-ray diffraction showed that the crystal was a mixture of 1:1  $\beta/\alpha$  mixed lactose crystal and  $\beta$ -lactose crystal. This confirmed that, to produce the 1:1  $\beta/\alpha$  mixed lactose crystal very low flow rates were required (1.5ml to 3ml/min flow rate). It was observed that the 1:1

$\beta/\alpha$  mixed lactose crystal was formed when the lactose solution formed a rubbery amorphous lactose solution and then quickly crystallized in the superheated steam environment. To confirm this hypothesis, spray dried amorphous lactose was crystallised over the roller dried inside the superheated steam environment at 125°C, 135°C and 145°C. The resulting product was a mixture of the 1:1  $\beta/\alpha$  mixed lactose crystal and  $\beta$ -lactose crystal. To produce an amorphous phase from the solution, the solution was injected in air for a few seconds before introducing it into the superheated steam environment. Lactose solution at 90 °C injected onto the roller with a temperature of 145°C for 10 sec in air and 15 minutes in superheated steam produced a crystal having a structure different to that of a  $\beta$ -lactose crystal or  $\alpha$ -lactose crystal and it had a similar X-ray diffraction pattern to that of the 1:1  $\beta/\alpha$  mixed lactose crystal documented in the literature and the crystal formed at Massey in 1997. It was also shown that in the absence of superheated steam,  $\beta$ -lactose crystals were formed.

It was clearly shown that a noticeable amount of the 1:1  $\beta/\alpha$  mixed lactose crystals are formed in products having  $\beta$ -lactose contents below 60%.

The formation of 1:1  $\beta/\alpha$  mixed lactose crystal was found to be very problematic and thus the results were not repeatable. Further investigation should be carried out with better control of all the parameters. Moisture content ( $m_c$ ) was thought to be a contributing factor that needs to be investigated further.

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# CHAPTER 1

## PROJECT OVERVIEW

A new lactose crystal was formed at Massey University, Palmerston North in 1997 by (Paterson & O'Donnell, 1997) while studying the effect of superheated steam on crystallization of lactose. This new crystal contained both  $\alpha$  and  $\beta$ -lactose anomers with a typical  $\beta$ -lactose content of 51-52% giving a  $\beta$ : $\alpha$  ratio of 1.08:1. It was found that the new crystal was produced under a superheated steam environment between temperatures 120°-155°C and above an initial drying rate of 0.35 gm/min/10ml. The present work attempts to develop a continuous process to produce the new lactose crystal.

Lactose is usually produced by crystallization from a lactose solution below 93.5°C followed by separation and flash drying, producing  $\alpha$ -lactose monohydrate crystals with a coating of amorphous lactose, or by crystallization above 93.5°C on a roller dryer producing a  $\beta$ -lactose crystal product with up to 30%  $\alpha$ -lactose incorporated into the  $\beta$ -lactose crystal structure. Amorphous lactose is produced when lactose solution is spray dried.

It was hypothesized that the new crystal could be produced by rapid crystallization at temperatures above 120°C. To create conditions for rapid crystallization it was proposed to initiate very fast drying producing amorphous lactose that would crystallize in a superheated steam environment to form the new crystal.

**The objectives of the present research work were:**

- Literature search to confirm that the crystal form found by (Paterson & O'Donnell, 1997) has not been documented before.
- Design and develop a process to obtain the required conditions to produce the new crystal continuously and verify the hypothesis made above.
- Produce 10 kg of the new crystal.
- Provided sufficient quantity of crystal was produced, determine the properties of the crystal- amorphous lactose content, dissolution time,

solubility limits, crystallinity, density, melting point, sweetness, crystal size and carry out tableting of the crystals.

- Use the results to compare the properties to those found by (Buma, 1978), (Lerk *et al.*, 1984 (a)), and (Paterson & O'Donnell, 1997).

Unfortunately the attempts at developing a continuous process failed due to some unknown factors which were producing a mixture of new crystal and  $\beta$ -lactose. Thus further investigations into the production of the new crystal are recommended. But the new crystal was produced once in a very small quantity. The X-ray diffraction pattern showed a different crystallographic structure than that of  $\beta$ -lactose and  $\alpha$ -lactose, and so it was concluded that this was a new lactose crystal. This thesis covers the process followed and modifications made to the set up during the project.

Firstly Chapter 2 covers the literature review. This was carried out to ensure that no process had been developed before to produce the new crystal. The literature search covered:

- Carry out a literature search to ensure that the crystal itself had not been discovered before.
- Different methods to produce lactose crystals or lactose additives.
- Detailed search of patented methods to produce lactose crystals or lactose tablet additives.
- The work done on the development of the new crystal at Massey University. The conditions required to produce the new crystal and the methods used to determine the properties of the new crystal.

Chapter 3 describes the step-by-step development of the continuous process. It includes the materials and methods, the results and discussions and the reasoning behind the changes made to the set up.

Chapter 4 ends the thesis with the conclusions and recommendations.