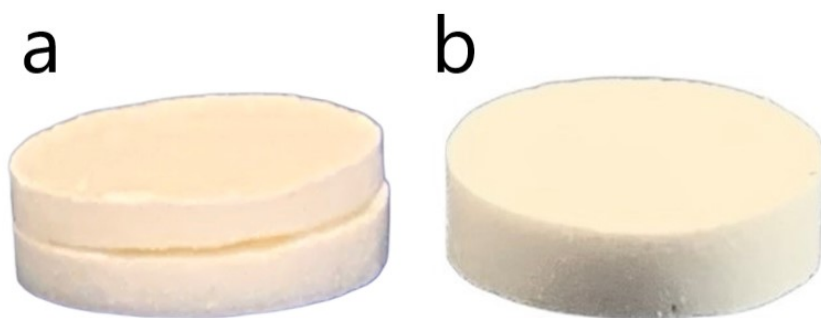


## **Supplementary material**

### **Supplementary material S-1**



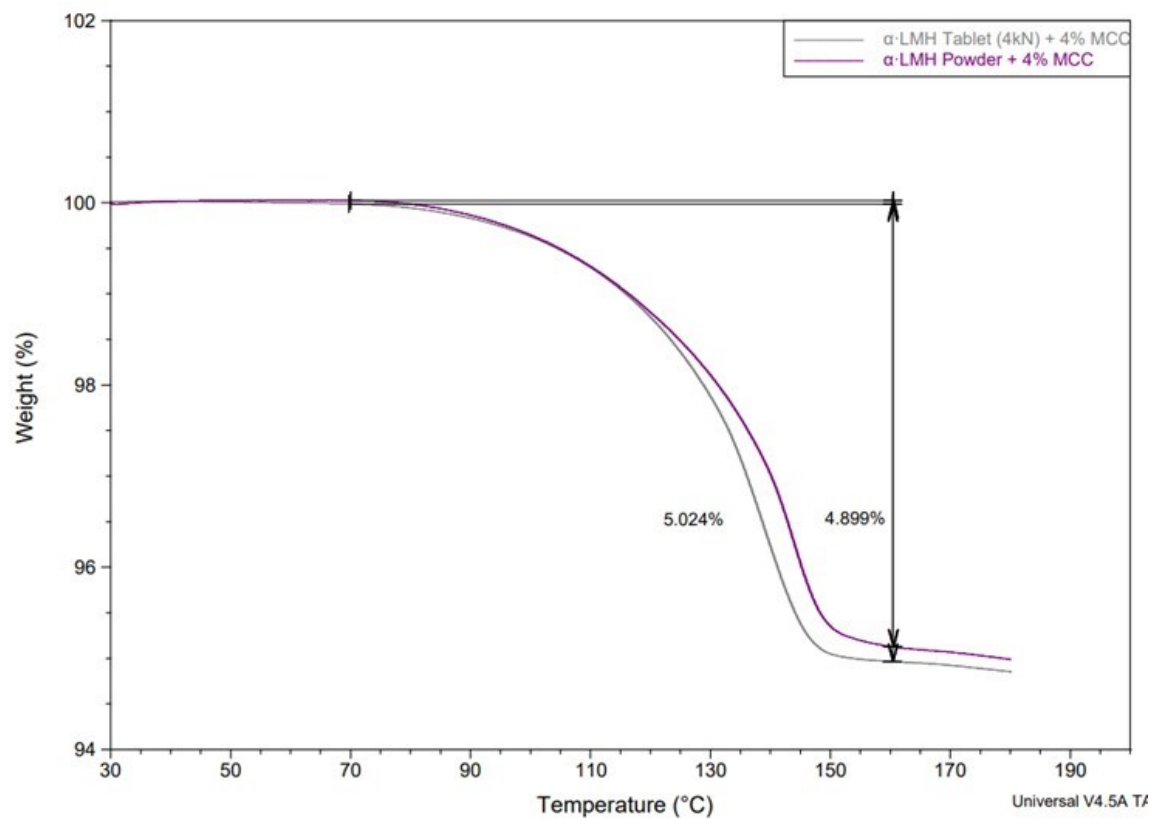
S-1: (a)  $\beta$  lactose (as received, 86.5%  $\beta$  anomer) tablets demonstrating ‘capping’ after compression and (b)  $\beta$  lactose as received + 4% MCC tablets, which remained intact after compression i.e. no ‘capping’.

## Supplementary material S-2

S-2: Characterisation of lactose tablets (plus 4% MCC) comprising lactose with different anomeric content. Data are presented as the mean  $\pm$ SD (n=10). \* Represents batches where some of the tablets initially included were rejected as having an unacceptable appearance and that were subsequently replaced (4 tablets in total).

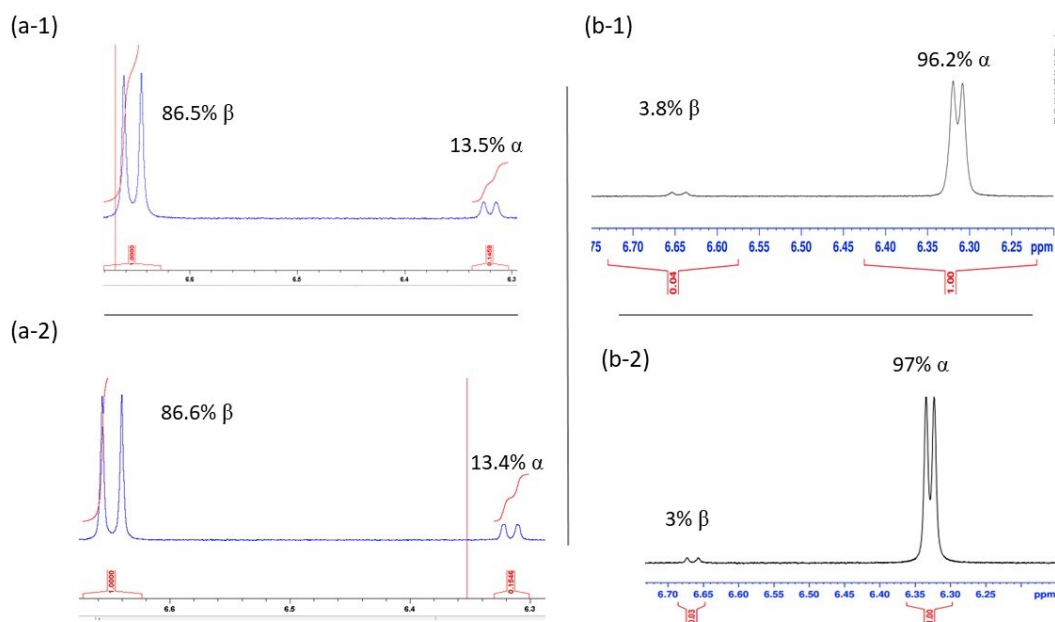
Tablet matrix	Compaction Force (kN)	Weight (mg)	Thickness (mm)	Diameter (mm)	Visual appearance
<b><math>\beta</math> lactose anhydrous (as received) – 13.5% <math>\alpha</math> anomer</b>	10	300.2 $\pm$ 1.9	3.0 $\pm$ 0.2	10.0 $\pm$ 0.6	Acceptable*
	20	299.9 $\pm$ 2.7	3.1 $\pm$ 0.1	10.1 $\pm$ 0.3	
	40	304.1 $\pm$ 4.9	2.9 $\pm$ 0.3	9.9 $\pm$ 0.2	
<b>lactose 35 days storage (40°C/60%RH) - 50.2% <math>\alpha</math> anomer</b>	10	305.5 $\pm$ 2.3	3.1 $\pm$ 0.2	10.1 $\pm$ 0.3	Acceptable
	20	300.5 $\pm$ 4.2	3.0 $\pm$ 0.1	10.1 $\pm$ 0.1	
	40	304.1 $\pm$ 3.5	2.8 $\pm$ 0.4	9.8 $\pm$ 0.2	
<b>lactose 60 days storage (40°C/60%RH) - 79.5% <math>\alpha</math> anomer</b>	10	296.4 $\pm$ 5.7	3.0 $\pm$ 0.2	10.1 $\pm$ 0.6	Acceptable
	20	303.12 $\pm$ 3.4	3.1 $\pm$ 0.1	10.2 $\pm$ 0.3	
	40	298.9 $\pm$ 1.7	2.9 $\pm$ 0.1	10.0 $\pm$ 0.8	
<b><math>\alpha</math>-LMH (as received) – 96.6% <math>\alpha</math> anomer</b>	10	298.2 $\pm$ 2.8	3.1 $\pm$ 0.1	10.2 $\pm$ 0.4	Acceptable*
	20	300.5 $\pm$ 4.4	3.1 $\pm$ 0.1	9.9 $\pm$ 0.4	
	40	304 $\pm$ 4.1	2.9 $\pm$ 0.2	10.1 $\pm$ 0.3	

### Supplementary material S-3



S-3: TGA thermogram comparison between  $\alpha$  lactose monohydrate tablet (grey) and powder (purple). Change in mass observed earlier with compressed tablet in contrast to powder.

## Supplementary material S-4



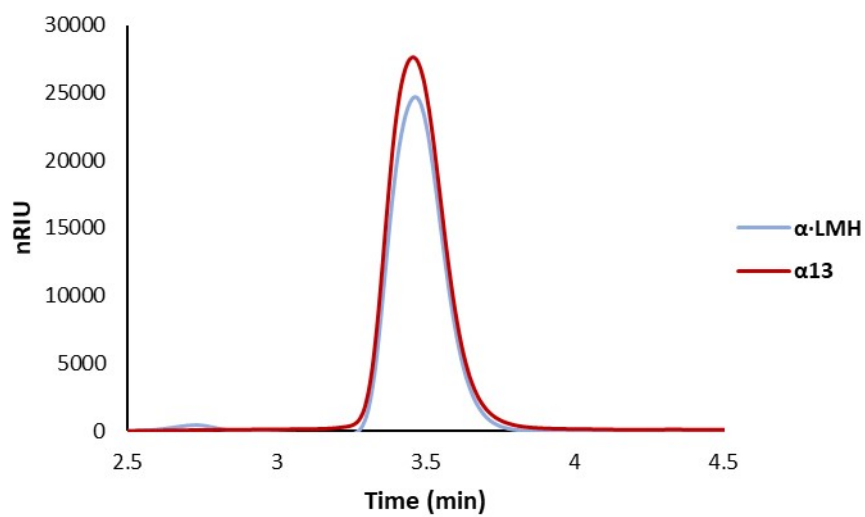
S-4:  $^1\text{H}$  NMR chemical shift of  $\beta$  lactose as received powder (a-1), compressed tablets of  $\beta$  lactose + MCC (a-2),  $\alpha$ -LMH powder as received (b-1) and compressed tablet of  $\alpha$ -LMH+ MCC (b-2).

## Supplementary material S-5

S-5: Crushing forces of tablets produced using three compression forces containing lactose comprised of powders with different  $\alpha/\beta$  ratios ( $n=10 \pm \text{SD}$ ).  $\alpha$  lactose monohydrate powders were subjected to identical durations and condition to the epimerised  $\beta$  anhydrous lactose prior to testing ( $40^\circ\text{C}/75\%\text{RH}$ ). Any significant difference between starting material (13.5%  $\alpha$  -  $\beta$  lactose as received) and tablets produced with powders stored for 35 or 60 days are marked by an asterix ( $p \leq 0.05$ ).

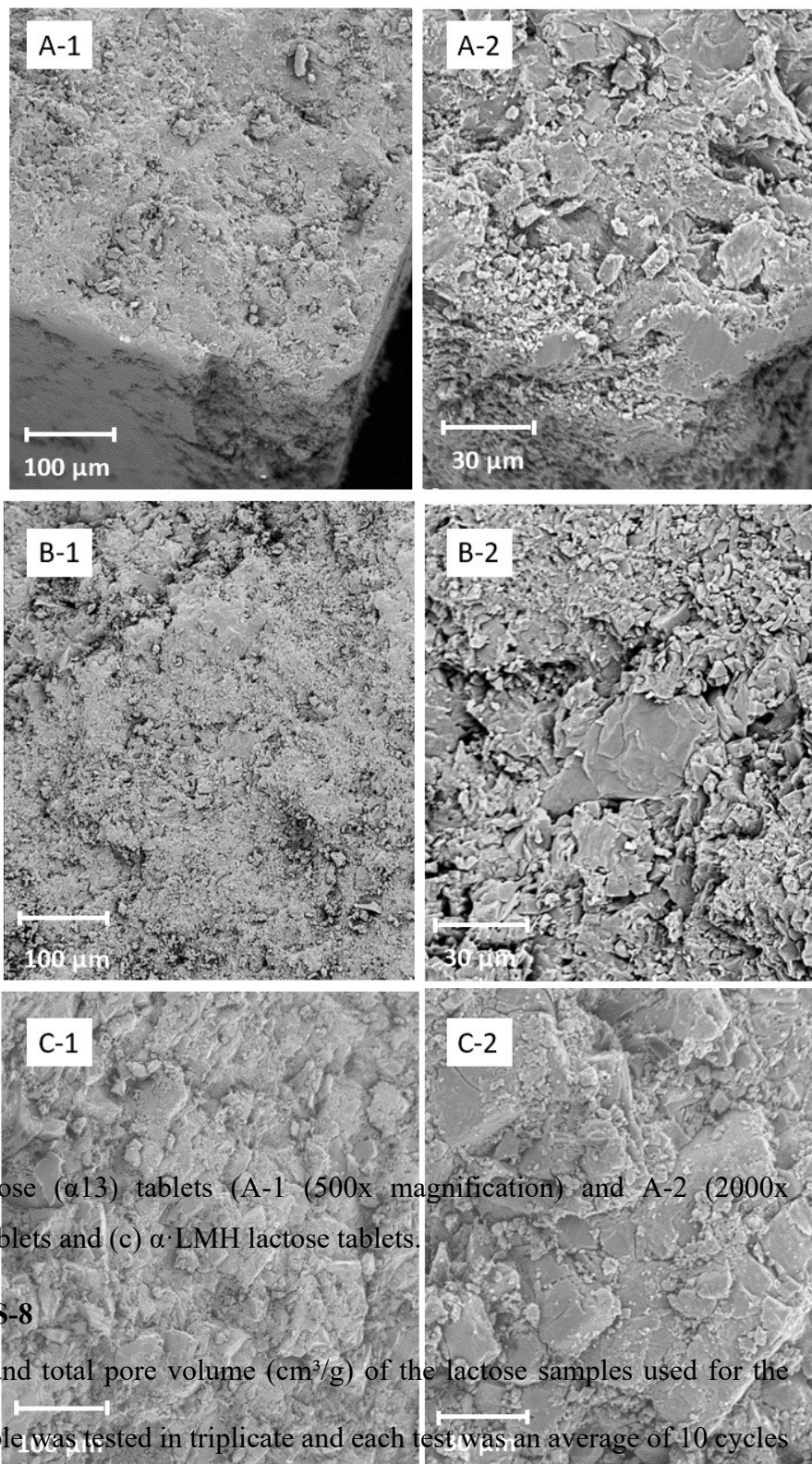
<b>Compression Force (kN)</b>	<b>13.5% <math>\alpha</math> - <math>\beta</math> lactose as received (N)</b>	<b>50.2 % <math>\alpha</math> anomer (N)</b>	<b>79.5% <math>\alpha</math> anomer (N)</b>
<b>10</b>	41.1 $\pm$ 1.8	40.3 $\pm$ 4	39 $\pm$ 4
<b>20</b>	122.9 $\pm$ 21	117.4 $\pm$ 9	142.1 $\pm$ 6*
<b>40</b>	170.2 $\pm$ 16	187 $\pm$ 24	207.4 $\pm$ 19 *
<b>Compression Force (kN)</b>	<b><math>\alpha</math> lactose monohydrate As received – 96.6% <math>\alpha</math> anomer)</b>	<b><math>\alpha</math> lactose monohydrate Stored for 35 days – 97.7% <math>\alpha</math> anomer)</b>	<b><math>\alpha</math> lactose monohydrate Stored for 60 days (98% <math>\alpha</math> anomer)</b>
<b>10</b>	46 $\pm$ 5	45.4 $\pm$ 4	45.7 $\pm$ 4
<b>20</b>	78.8 $\pm$ 10.4	76.1 $\pm$ 6.6	70.4 $\pm$ 10.4
<b>40</b>	127.3 $\pm$ 17.7	117.1 $\pm$ 18.7	127.8 $\pm$ 13.5

### Supplementary material S-6



**S-6:** Comparative RI chromatogram between  $\alpha$  lactose monohydrate (blue) and  $\beta$  lactose as received powders (red).

# Supplementary material S-7



S-7: (A) SEM of  $\beta$  lactose ( $\alpha$ 13) tablets (A-1 (500x magnification) and A-2 (2000x magnification)), (B)  $\alpha$ 79 tablets and (c)  $\alpha$  LMH lactose tablets.

## Supplementary material S-8

S-8 True density ( $\text{g}/\text{cm}^3$ ) and total pore volume ( $\text{cm}^3/\text{g}$ ) of the lactose samples used for the tabletting study. Each sample was tested in triplicate and each test was an average of 10 cycles

( $n=30$ ). \* Represents statistical difference with the starting material ( $\beta$ -lactose as received). +

Represents data less than 3 decimal places.

Sample	True Density ( $\text{g}/\text{cm}^3$ )	$\pm$ SD	Total Pore volume ( $\text{cm}^3/\text{g}$ )	$\pm$ SD
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<b>'β lactose' (i.e. containing 13.5%-α-lactose as received)</b>	1.579	0.001	0.366	0 <sup>+</sup>
<b>50.2% α lactose</b>	1.552*	0 <sup>+</sup>	0.355*	0 <sup>+</sup>
<b>79.5% α lactose</b>	1.546*	0 <sup>+</sup>	0.353*	0 <sup>+</sup>
<b>α-LMH</b>	1.541	0 <sup>+</sup>	0.351	0 <sup>+</sup>
<b>Acetylsalicylic Acid (ASA)</b>	1.384	0 <sup>+</sup>	0.277	0 <sup>+</sup>

**Supplementary material S-9**



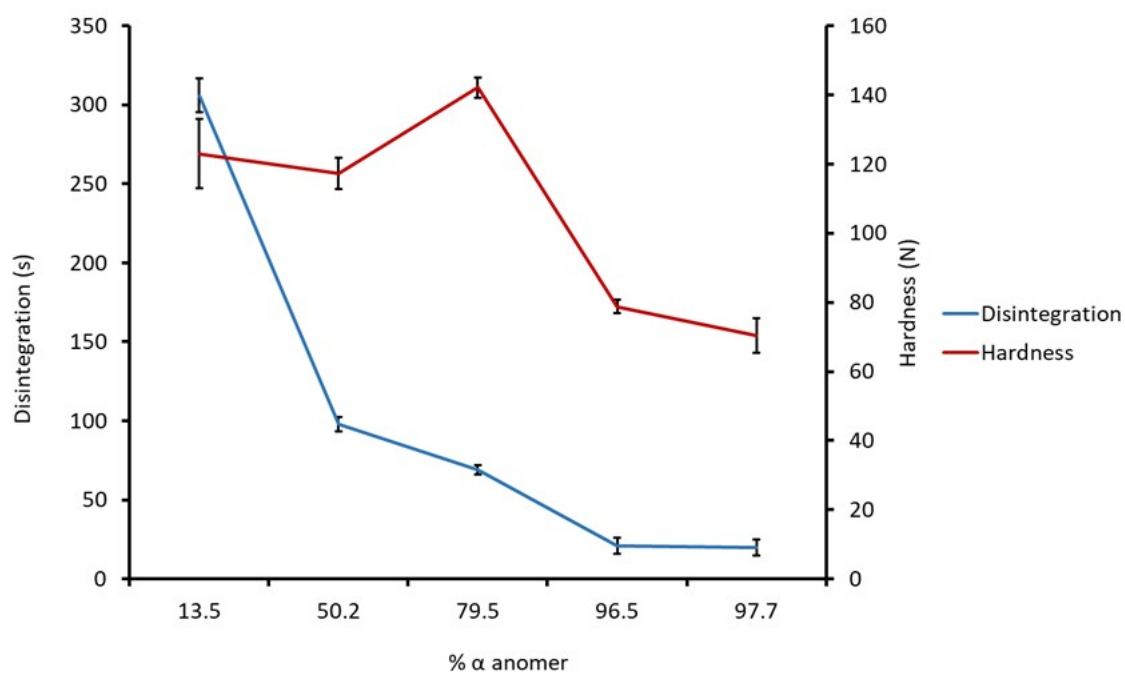
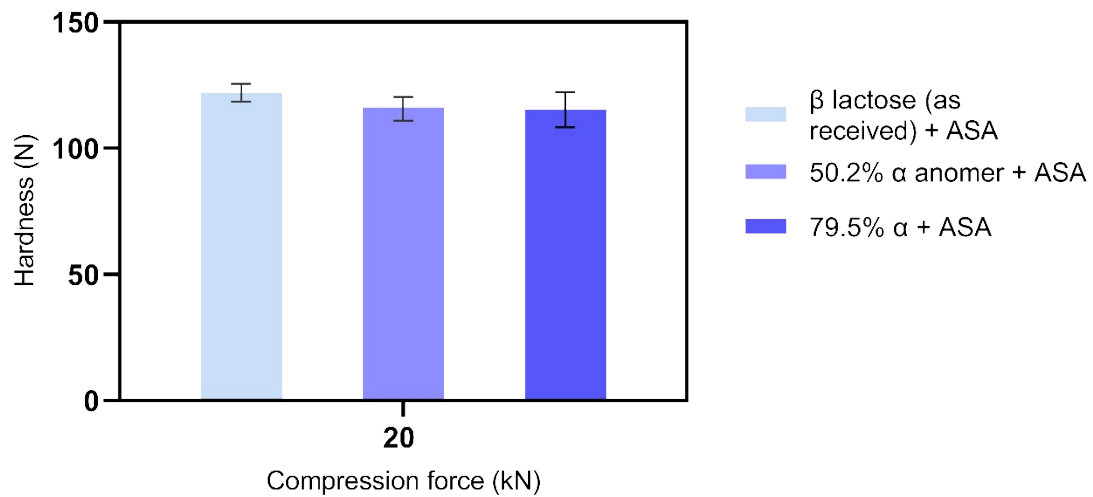


Figure S 9: Comparison between hardness properties (red) and disintegration times (blue) of tablets prepared using a compression force of 20 kN. The x-axis represents the  $\alpha$  anomeric content of tablets,  $\beta$  lactose as received (13.5%  $\alpha$ ),  $\alpha$ 50,  $\alpha$ 79.5,  $\alpha$ ·LMH as received (96.5 %  $\alpha$ ) and  $\alpha$ ·LMH stored for 60 days at 40°C/75% RH (97.7%  $\alpha$ ).

# Supplementary material S-10



S-10: Hardness properties of tablets containing different anomeric content of lactose + ASA (1:1 ratio).  $\pm$ SD ( $n=10$ ). No statistical differences were recorded.