Effect of age and fermentation on postprandial serum and urine metabolites after consumption of milk and yogurt in healthy young and old men

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INTRODUCTION

Fermentation of food has been a widely used method of natural preservation for thousands of years. Fermented dairy products represent a major fraction of the consumed fermented foods. Their potential health benefits, in addition to their nutritional properties, made them an attractive fermented food group for research. In the present study, the influence of cow's milk fermentation on the postprandial response of healthy young and old adult men was investigated in serum and urine.

OBJECTIVES

- Effect of elimination of dairy products and limited consumption of fermented non-dairy foods
- Monitor the postprandial metabolites measured with GC-MS in serum and urine after a single intake of 600 mL milk and yogurt
- Observe the influence of fermentation by comparing whole milk and yogurt
- Effect of age on the postprandial metabolome

EXPERIMENTAL

Randomized controlled crossover study

- 14 healthy young (YA, 20-35 y) and 14 old (OA, 65-80 y) adult men
- 3 weeks run-in period, without consumption of dairy products and limit the consumption of fermented non-dairy foods (restriction phase)
- Intervention with a single dose of 600 mL whole milk *vs* yogurt
- Blood serum sampling postprandially at 0, 15, 30, 60, 90, 120, 180, 240, 300 and 360 min
- Urine fasting, 0-3 h and 3-6 h pool

Metabolomic analysis

GC-MS workflow

- Two step derivatization (methoximation and trimethylsilylation)
- Untargeted GC-MS analysis
- Selection of postprandial active compounds
- Manual integration of selected compounds
- Statistical evaluation

RESULTS

In serum and urine samples, 21 interesting metabolites could be identified and quantified. 14 amino acids, two amino acid derivates, one fatty acid, lactose, and three lactose metabolites were quantified.

After the three-week restriction phase lactose, galactose, galactitol and indole-3-lactic acid were reduced in the fasting morning urine. Alanine, asparagine, aspartic acid, isoleucine, leucine, methionine, serine, threonine, and valine were elevated in the fasting morning urine after the restriction phase. These effects could not be observed in the fasting serum samples. 3-Indoleacetic acid, indole-3-lactic acid, lactose, leucine, tyrosine and valine were slightly, although significantly, reduced in fasting serum samples after the restriction phase.

Aspartic acid (only in serum), threonine (only in urine), indole-3-lactic acid, lactose, galactitol and galactonate showed a significant postprandial product effect in serum and urine samples, their response to milk and yoghurt ingestion being different. Tyrosine and lactose showed a significant postprandial age effect in serum samples, their response to dairy ingestion differing in the young and old adult group. Also asparagine and galactonate showed a significant postprandial age effect in urine samples. Lactose shows significantly higher postprandial variability in serum and urine after milk and yoghurt ingestion in older men.

Table 1: Significant postprandial metabolites in serum (median iAUC) and urine (median 0-6 h) in young men (YA) and old men (OA) after consumption of milk and yogurt.

Metabolite	Serum						Urine					
	Milk		Yogurt		Effect		Milk		Yogurt		Effect	
	OA	YA	OA	YA	Age	Prod	OA	YA	OA	YA	Age	Prod
3-Indoleacetic acid	-0.6	-1.3	-0.8	-0.8			1.1	0.6	0.0	0.4		
Alanine	0.4	0.5	1.3	1.3			0.6	1.1	1.3	2.1		
Asparagine	1.5	1.4	1.8	0.8			-0.4	-2.0	-0.1	-0.7	*	
Aspartic acid	0.9	1.5	0.5	0.8		*	-1.4	-1.5	-1.0	-1.0		
Cysteine	1.6	4.4	2.3	2.0			-1.7	-3.2	-2.0	-2.0		
Galactitol	4.1	3.9	2.3	2.9		*	3.4	3.3	2.1	2.3		*
Galactonate	7.7	6.3	5.7	4.8		*	5.4	6.3	4.0	5.6	*	*
Galactose	9.1	6.5	8.6	6.3			9.6	9.4	8.0	10.2		
Glycine	0.0	0.4	0.1	-0.5			1.2	1.1	1.5	1.2		
Heptadecanoic acid	0.3	-0.3	0.7	0.2			0.1	0.1	0.1	0.3		
Indole-3-lactic acid	-0.4	-0.6	-0.2	-0.2		*	-1.0	-0.8	-1.8	-0.5		*
Isoleucine	2.0	1.9	1.9	1.1			0.0	-0.3	-0.6	0.2		
Lactose	6.7	5.0	3.3	2.2	*	*	7.0	5.5	2.8	2.6		*
Leucine	1.5	1.2	1.3	0.8			0.7	-0.1	0.1	2.2		
Lysine	1.1	0.7	0.8	1.1			2.6	3.5	2.8	4.2		
Methionine	1.4	2.0	1.5	1.6			0.0	-1.2	-0.2	0.3		
Phenylalanine	1.0	0.7	1.0	0.6			-0.7	-2.2	-1.8	-1.3		
Serine	1.0	2.4	1.3	1.1			0.4	-0.9	0.4	1.1		
Threonine	0.6	1.8	0.9	1.5			1.2	0.8	1.2	1.8		*
Tyrosine	0.8	0.4	1.0	0.7	*		-0.3	-0.6	0.7	-0.1		
Valine	0.7	0.3	0.6	0.7			0.1	-0.4	-0.8	0.1		

Legend: * p < 0.05 significant effect of age and/or product

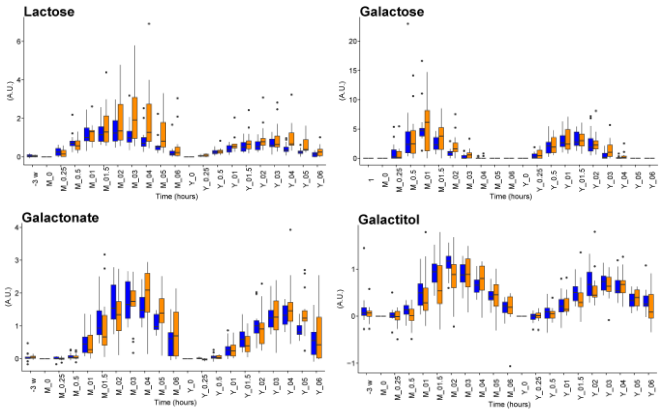

Figure 1: Kinetic of lactose, galactose, galactonate and galactitol in serum of ■ young men and ■ old men after consumption of milk (M) and (Y)

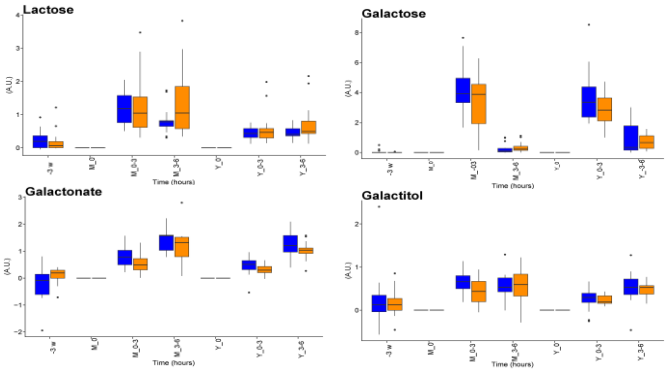

Figure 2: Kinetic of lactose, galactose, galactonate and galactitol in urine pools of ■ young men and ■ old men after consumption of milk (M) and (Y)

CONCLUSIONS

The elimination of dairy products and the reduction of fermented foods in the restriction phase reduced the markers of these foods (e.g. lactose and indole-3-lactic acid) in fasting serum and fasting morning urine. The postprandial response of metabolites in serum and urine after consumption of a single intake of 600 mL milk and yogurt was very similar in the two age groups. Only seven metabolites showed a significant product and/or age effect. Lactose malabsorption may increase with age. In this respect, lactose ($p < 0.05$) and its metabolites ($p > 0.05$) showed greater variability in older men than in young men in our study, indicating a heterogeneous loss of lactase activity with age. Further research is needed to better understand the effects of age on the metabolome after consumption of dairy and other foods.

References:

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This trial was registered at clinicaltrials.gov as NCT03500003.

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