Zeitschrift für
Ernährungswissenschaft Z Ernährungswiss 30:131–137 (1991)

Postprandial plasma D-lactate concentrations after yogurt ingestion

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Zusammenfassung: Das Risiko einer D-Laktat-Azidose durch Joghurtverzehr wurde bei 7 gesunden Probanden untersucht. Nach dem Verzehr von Joghurt, der eine Aufnahme von 1,06 mmol/kg Körpergewicht D-Milchsäure bewirkte, stiegen die postprandialen Plasma-D-Laktat-Spiegel innerhalb von 60 min von 0,070 ± 0,020 auf einen Höchstwert von 0,200 ± 0,010 mmol/l an. Ein doppelt so hoher Anstieg der postprandialen Plasma-D-Laktat-Konzentrationen wurde nach Verabreichung der äquivalenten Menge D-Milchsäure in Form einer wäßrigen Lösung von DL-Laktat beobachtet. Die postprandialen Plasma-D-Laktat-Maxima fielen nach Joghurt flacher und breiter aus, während die Kurvenflächen unabhängig von der Zufuhrform waren. Nach dem Verzehr von 0,64 mmol/kg Körpergewicht D-Milchsäure in Joghurt stiegen die D-Laktat-Konzentrationen im Plasma bis auf 0,086 ± 0,030 mmol/l an. Anzeichen einer geringfügigen, vorübergehenden, kompensierten metabolischen Azidose nach Zufuhr der wäßrigen D-Milchsäure-Lösung wurden nach Verzehr von Joghurt nicht beobachtet. Aus diesen Ergebnissen wird der Schluß gezogen, daß der Verzehr D-Milchsäure-haltiger Lebensmittel für gesunde Erwachsene unbedenklich ist.

Summary: The risk of D-lactic acidosis after consumption of yogurt was investigated in seven healthy volunteers. After ingestion of yogurt containing 1.06 mmol/kg body weight, D-lactic acid postprandial plasma D-lactate concentrations increased from 0.070 ± 0.020 to a maximum of 0.200 ± 0.010 mmol/l within 60 min. That was half the maximum concentration after the equivalent amount of D-lactate in the form of an aqueous solution of DL-lactate. The shape of the postprandial plasma D-lactate peak was flatter, but much broader after yogurt than after the aqueous solution, the peak areas being equal. When 0.64 mmol/kg body weight D-lactate were consumed as yogurt, plasma concentrations amounted to 0.086 ± 0.030 mmol/l. Signs of a mild, transient, compensated metabolic acidosis, which was apparent in case of the aqueous lactic acid solution did not occur in case of yogurt. It is concluded that the consumption of foods containing D-lactic acid gives no reason for concern in healthy adults.

Schlüsselwörter: D-Laktat, Joghurt, Mahlzeiteneinfluß

Key words: D-lactate; yogurt; ingestion effects

Introduction

Due to the absence of a specific dehydrogenase, D-lactic acid is metabolized in man slower than is the L-enantiomer (3, 4, 7, 8, 11) and, at

most, very small quantities of this acid are formed endogeneously by host metabolism (14).

D-lactic acid is contained in some fermented foods like yogurt, kefir, pickles or sauerkraut, but is also contained in cheese, meat, meat products and sausages, in red wine, or as a food additive in other foodstuffs (22). Another source of D-lactic acid is the activity of intestinal bacteria. Excessive microbial D-lactic acid production causes severe and sometimes fatal acidosis in ruminants after carbohydrate overfeeding (5, 9) and in patients as a complication of the "short bowel syndrome" (13, 17, 18, 20, 21).

Indications that D-lactic acid exerts metabolic stress (8, 10, 16) led to widespread supposition about detrimental health effects of D-lactic acid and about consumption of foods containing D-lactate. Such effects were not confirmed in a recent investigation (23). In these experiments as much as 2.2 mmol/kg body weight D-lactic acid, orally administered as an aqueous solution of DL-lactate, were eliminated fast enough from the plasma compartment to avoid both short-term and long-term accumulation, thus excluding the risk of D-lactic acidosis.

Normally, D-lactic acid is not consumed as an aqueous solution, but within a meal together with other nutrients. Some components of a meal, like osmotically active carbohydrates, amino acids, fat or acids delay the time of gastric emptying (15), possibly affecting kinetics of D-lactate absorption. It was the purpose of this study to investigate postprandial plasma D-lactate concentrations after a D-lactate-containing "real" meal, and to elucidate the actual health risk caused by consumption of foods containing D-lactic acid.

Materials and methods

Seven healthy, informed volunteers participated in this study. The group of subjects included members of the Federal Dairy Research Center, Kiel (one female, six male). Their average age was 34.3 (range 26–51) years, their mean body weight was 66.1 ± 3.3 kg. All subjects maintained their usual diets with the exception of the experiment.

On experimental days, at 0900 hours they consumed (after an overnight fast) between 800 and 1600 g of a commercial yogurt within 20 min, instead of their usual breakfast. The yogurt was without fruit-additives or sugar; its pH was 3.9. The brand was selected with respect to a high content of D-lactic acid. Exact D-lactate concentrations were estimated in aliquots of each yogurt. D- and L-lactate concentrations in the yogurt were such that, on the average, 0.64 ± 0.06 or 1.06 ± 0.08 mmol/kg body weight D-lactic acid and 0.76 ± 0.07 or 1.28 ± 0.09 mmol/kg body weight L-lactic acid were contained in one meal. These doses amounted to 57 % and 96 %, respectively, of the maximum amount allowed by a former FAO/WHO recommendation (23).

In a control experiment the volunteers drank a solution of 2.22 mmol/kg body weight DL-lactic acid (1.11 mmol/kg body weight D-lactic acid) in 500 ml water, followed by 1 l water within the next 30 min. DL- and L-lactic acid were preparations from Boehringer (Ingelheim, Germany); by-products were hydrolyzed by dilution with water and boiling. The pH of the solutions were adjusted to 3.6 with about 100 mmol/l NaOH.

Blood was drawn from the vena cephalica before and up to 360 min after drinking. The pH, $[HCO_3]^-$, and pCO_2 were measured according to Astrup's procedure (1). D- (6) and L-lactic acid (12) were estimated enzymatically in neutralized aliquots of the

blood samples, which had been deproteinized with perchloric acid and stored at −20 °C.

The results are expressed as mean ± SEM. Statistical differences were assessed by the Mann-Whitney test by ranks.

Results

Side effects

No side effects were observed when 0.64 and 1.06 mmol/kg body weight D-lactic acid were consumed as yogurt. One test subject (of Japanese extraction) ate only the test meal containing the lower dosis of D-lactate, and was identified as a lactose malabsorber via determination of postprandial plasma galactose, but reported no side effects. On the other hand, some diarrhea was reported by two subjects after the aqueous solution of DL-lactic acid. This did not seem to be a specific effect of D-lactate, because the same symptoms could be produced by drinking the corresponding amount of pure L-lactic acid (Boehringer Ingelheim, Germany) solution.

D-lactate

Figure 1 shows the plot of plasma D-lactate concentrations before and 6 h following consumption of yogurt containing 0.64 or 1.06 mmol/kg body weight D-lactate, or of the aqueous solution of 1.11 mmol/kg body weight D-lactic acid, respectively.

When the aqueous solution was given to the subjects, plasma D-lactate concentration rose to a sharp maximum of 0.38 ± 0.02 mmol/l within 40

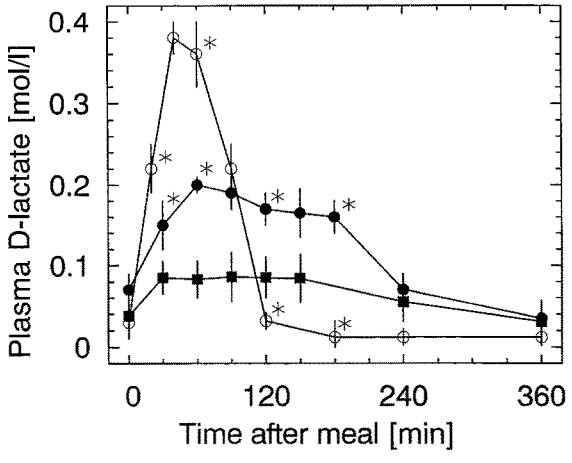

Fig. 1. Plasma D-lactate concentrations before and after ingestion of 0.64 (■–■, n = 7) and 1.06 mmol/kg body weight (●–●, n = 4) D-lactic acid in yogurt and of an aqueous DL-lactate solution containing 1.11 mmol/kg body weight D-lactic acid (○–○, n = 7) by healthy volunteers after an overnight fast. Samples were taken from venous blood. Plots represent mean ± SEM. Asterisks mark significant differences between aqueous solution and yogurt at the $p < 0.01$ level.

Table 1. Areas under the postprandial plasma D-lactate response curves after D-lactic acid ingestion by healthy volunteers.

D-lactic acid ingested	n	Plasma D-lactate (mmol · min/l)	
		Mean	SEM
0.64 mmol/kg body weight in yogurt	7	14.8	5.0
1.06 mmol/kg body weight in yogurt	4	30.3	2.8
1.11 mmol/kg body weight aqueous solution	7	31.8	3.0

min and decreased thereafter (with a half-life of 28.6 ± 4.3 min) to basal levels. In contrast, consumption of the same amount of D-lactic acid in yogurt resulted in a broad peak from the 60th to 240th min, with a maximum concentration of about one-half of the former value, namely 0.20 ± 0.01 mmol/l, the difference being significant. When half the amount of yogurt was ingested, the maximal concentration decreased by 50 % to 0.09 ± 0.03 mmol/l, the length of the maximum being unchanged. Following yogurt consumption, fasting levels of plasma D-lactate were reached 6 h after the test meals.

The same areas under the time-concentration curves of plasma D-lactate were observed following ingestion of 1.06 mmol/kg body weight D-lactic acid in an aqueous solution and in yogurt (Table 1). When 0.64 mmol/kg body weight D-lactate in yogurt were consumed the areas under the curves were also 50 % smaller.

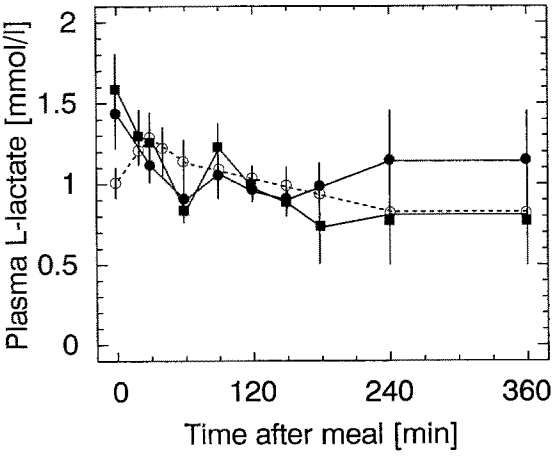

Fig. 2. Plasma L-lactate concentrations before and after ingestion of 0.76 (■–■, n = 7) and 1.28 mmol/kg body weight (●–●, n = 4) L-lactic acid in yogurt and of 1.28 mmol/kg body weight (○–○, n = 7) aqueous L-lactate. Same conditions as in Fig. 1.

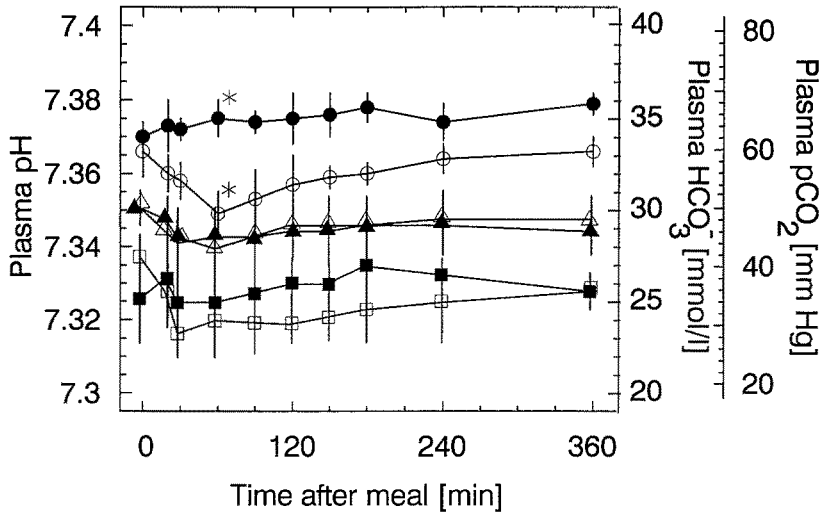

Fig. 3. Time-course of pH, bicarbonate, and pCO_2 in venous blood of healthy volunteers after ingestion of 1.06 mmol/kg body weight D-lactic acid in yogurt, or as an aqueous solution of 1.11 mmol/kg body weight DL-lactate. Yogurt meal: pH (●–●), HCO_3^- (■–■), pCO_2 (▲–▲); aqueous solution: pH (○–○), HCO_3^- (□–□), pCO_2 (△–△). Plots represent mean ± SEM. Asterisks mark significant differences between aqueous solution and yogurt at the $p < 0.05$ level.

L-lactate

Plasma levels of L-lactate following ingestion of yogurt or the aqueous solution of DL-lactic acid are represented in Fig. 2. Fasting levels ($t = 0$) were not significantly different between the groups consuming either L-lactate as an aqueous solution or the equivalent amount in yogurt.

pH and bicarbonate

As shown in Fig. 3 there was a transient decrease in plasma pH and bicarbonate only after aqueous lactic acid, the drop in pH of 0.01 being non-significant compared to $t = 0$. No decrease at all in pH was observed after yogurt. Differences between diets were significant only at $t = 60$ min when the pH in the group consuming the aqueous solution was at its lowest value.

Discussion

The most important result of the present study was, briefly: when D-lactic acid is not consumed in the form of an experimental aqueous solution of the pure acid, but simultaneously ingested with other nutrients, for example, in yogurt, there is a significant lower and broader postprandial plasma D-lactate concentration curve.

Due to the simultaneous occurrence of peak broadening and a decrease of the maximum D-lactate concentration, it is improbable that the kinetics

of D-lactate elimination from the plasma compartment was altered by yogurt consumption. Peak broadening would indicate delayed elimination, whereas the decrease of maximum concentration would signify the contrary, namely an increased rate of elimination of D-lactate from plasma.

On the other hand, D-lactate absorption from yogurt seems not to be reduced, because after ingestion of both the aqueous solution and yogurt the same total amount of D-lactate appeared in the plasma, as verified by equal areas under the time-concentration curves.

The flat and broad postprandial concentration maximum of D-lactate after yogurt indicates, most probably, a delay in intestinal passage. This may be due to the higher osmolality of the yogurt, its acidity, its fat content, or to free amino acids. All these factors are acting in the same direction, causing a delay in gastric emptying (15).

As a result of the considerable amount of acid administered to the subjects there were signs of a mild compensated metabolic acidosis when the aqueous solution of DL-lactate was ingested, namely a non-significant drop in plasma-pH of short duration and a transient decrease in plasma bicarbonate. When yogurt was consumed not even the slightest drop in pH was observed, probably not only due to the smaller increase in plasma D-lactate, but also as a result of the decrease in postprandial plasma L-lactate compensating for the increase of D-lactic acid.

In a previous study, we concluded from experiments with aqueous DL-lactate in healthy volunteers (23) that the consumption of considerable amounts of D-lactate has no harmful effects. The present investigation further substantiates this conclusion and demonstrates that, when D-lactic acid is given in a meal, the presence of other nutrients diminishes the risk of D-lactic acidosis even more. Analogous beneficial effects are seen, for example, with lactose intolerant subjects, who reported reduced intolerance symptoms when lactose was consumed during a meal (19).

We reported earlier that D-lactate in plasma did not accumulate after its chronic ingestion (23) and that no case of a nutrition-dependent D-lactic acidosis in humans has been reported until now (2). Clinical investigations in patients with short-bowel syndrome and D-lactic acidosis did not unequivocally establish a specific D-lactate toxicity (18). This body of evidence together with the data reported herein lend further support to the conclusion that there is no reason for concern about the consumption of D-lactic-acid-containing foods by healthy adults.

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Received October 10, 1990

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