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Energy Values of Lactitol and Lactulose as Determined with Miniature Pigs and Growing Rats

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ABSTRACT

Digestible and metabolisable energy values were determined by the metabolic balance method. The mean (and SEM) metabolisable energy values for lactitol were 11·8 (0·8) and 9·8 (1·5) kJ g^{-1}, respectively, for the laboratory rat and the miniature pig. For lactulose, metabolisable energy values were 8·4 (1·0) and 9·0 (0·8) kJ g^{-1}, respectively, for the rat and pig. Digestible energy values were little different from these metabolisable energy values indicating that the efficiency of utilisation of the digestion products absorbed may be high.

Key words: Lactulose, lactitol, metabolisable energy, digestible energy, laboratory rat, miniature pig.

INTRODUCTION

This paper describes the determination of energy values by the energy balance procedure of lactitol (4-O-β-D-galactopyranosyl-D-sorbitol) and lactulose (4-O-β-D-galactopyranosyl-D-fructofuranose), both derivatives of lactose. It is assumed that in most mammals these carbohydrates are hydrolysed only very slowly if at all (Dahlqvist and Gryboski 1965; Nilsson and Jägerstad 1987). It has been proposed that lactitol could be used in the manufacture of 'low calorie' foods (van Velthuijsen 1979), and indeed it was recently approved for food use in the UK. However, there is

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little published information on its contribution to energy value. Lactulose has found medical applications as a laxative (Mayerhofer and Petuely 1959) and is used in the treatment of portal systemic encephalopathy (Bircher *et al* 1966). It may be prescribed in considerable daily quantity (20 to 100 g or more), but the contribution of this sugar to the energy metabolism of the patient has been given little consideration and no energy values are available.

EXPERIMENTAL

Materials

The lactitol preparation, hereinafter called lactitol, was a preparation of lactitol monohydrate kindly supplied by CV Chemie Combinatie Amsterdam CCA (Gorinchem, The Netherlands), and the lactulose preparation, hereinafter called lactulose, was Duphalac, a syrup containing 0·67 g lactulose, 0·11 g galactose and 0·06 g lactose per ml (Duphar BV, Amsterdam, The Netherlands).

Determinations with pigs

Experimental animals

Six female miniature pigs of the Göttingen strain were used. They were 11 weeks old at the start of the experiment and weighed 3·4–7·0 kg.

Dietary treatments

In the first experiment the treatments were a control diet (a normal pig starter diet) and an experimental treatment in which lactitol was added to each meal of starter diet prior to feeding in the ratio 1 part lactitol to 10 parts starter diet. In both treatments, starter diet was provided on the same scale based on body weight (18 g food kg^{-1} body weight) and given as a slurry mixed with water. The daily ration was given in two halves, at 09.30 and 16.30 h. The composition of the starter diet (g kg^{-1}) was 249 barley meal, 163 fat mixture (Megalac, Volac Ltd, Royston, UK), 140 wheat meal, 134 soya bean meal, 110 skim milk powder, 110 white fish meal, 68 maize meal, 13 dicalcium phosphate, 5 sodium chloride, 4 trace mineral mixture, 4 vitamin mixture. The protein content (N × 6·25) was 218 g kg^{-1}. Water was available throughout the experiment.

In the second experiment the same starter diet was used and, again, given according to body weight. Supplements of a control solution (control treatment) or Duphalac (experimental treatment) were added to each meal before feeding. The amount of Duphalac depended on the tolerance of the individual pig and ranged from 276 to 465 ml kg^{-1} of starter diet. The control solution contained galactose and lactose in the same concentrations as in Duphalac, and its purpose was to equalise intakes of these sugars.

Housing

The pigs were individually housed at 22°C in specially designed metabolism cages which allowed separate and total collection of faeces and urine (Ratcliffe and Fordham 1987).

Experimental design

A cross-over design with two experimental periods was used. The pigs were divided into two equal groups (three pigs per group) using a table of random numbers. One group received experimental treatment and the other had the control treatment in the first experimental period; the treatments were switched for the second experimental period so that each pig was its own control. For lactitol (first experiment) the experimental periods lasted 7 days. The pigs were weighed on the first day of each period, and new levels of feeding were introduced according to changes in body weight. A 4-day period of adaptation to the diets then followed. The balances were started before the first feed on day 5 and lasted for 3 days—ending before the first feed on day 1 of the next experimental period. The treatments were then switched and the second adaptation period started. Separate collections of faeces and urine were made twice daily during the balance periods and stored in plastic bottles under 0·05 M sulphuric acid at 4°C. At the end of a balance, the bulked faeces and urine were stored at −20°C. In the second experiment (on lactulose) the adaptation period was extended to determine the maximum quantity of Duphalac each pig would consume with the production of soft faeces but without scouring. Otherwise, feeding and other experimental details followed the same routine as adopted in the first experiment.

Determinations with rats

Experimental animals

For the third experiment, 12 female rats were selected from the Laboratory's colony of Lister Norwegian hooded rats. The rats were 6 weeks old at the beginning of the experiment and weighed 150–170 g. Six female rats from the same colony were used in the fourth experiment. At the start they weighed 103–121 g.

Dietary treatments

In the third experiment the diets contained 900 parts by weight of a basal mixture:

maize starch 520 g
casein 119 g
ground sucrose 100 g
Solkafloc 50 g
maize oil 50 g
salt mixture (Achinewhu and Hewitt 1979) 50 g
vitamin mixture (US Pharmacopeia 1965) 10 g
Rovimix E_{250} (containing 250 mg α-tocopheryl acetate g^{-1}; Roche Products, Welwyn Garden City, Herts) 0·24 g
cyanocobalamin (in a solution containing 100 μg ml^{-1}) 2 μg

and 100 parts of maize starch in the control diet or 100 parts lactitol in the experimental diet. The same basal mixture was used in the fourth experiment. Each 900 parts of it was mixed with 50 or 75 parts of lactulose (in the form of Duphalac) and made up to 1000 parts with maize starch. The control diet contained 900 parts of basal, galactose and lactose, equivalent to the amounts in the Duphalac supplements, and maize starch to 1000 parts.

Throughout the third experiment the rats were given 12 g food daily at 09.30 h while in the fourth experiment they were given 10 g daily in the first period and 11 g in the second period.

Housing
During balance periods, the rats were individually housed in metabolism cages (Techniplast, Buguggiate, Italy) which allowed the separate and total collection of faeces and urine. Prior to this, the rats were individually housed in holding cages. The rats were kept in a constant temperature room at 22°C.

Experimental design
This was essentially the same as for the pig experiments. Sulphuric acid (2–3 ml 0·05 M) was placed in the vessel for collecting the urine to reduce losses of nitrogen. Contamination of the urine with food occurred very occasionally and was removed by filtering through Whatman filter paper (No 1).

Sample processing and analysis

The bulked faeces were freeze dried (Virtis Freeze-Drier model 50SR) and the dry weight was recorded. The dried faecal matter was then homogenised in a domestic food processor and stored in a desiccator over silica gel. Samples were taken for total N estimation by a micro-Kjeldahl method and for gross energy in an adiabatic bomb calorimeter (Gallenkamp, London) standardised using benzoic acid. The total urine collection was thawed, thoroughly mixed and weighed and a sample was removed for analysis of total N. Urine samples were prepared for bomb calorimetry by pipetting 10–20 ml on to a sheet of polythene film (cling film: 15 × 15 cm; Payne Scientific, Slough) placed in a 25-ml beaker and freeze drying. The dried urine sample was then wrapped in the polythene film and stored in a desiccator, also over silica gel. Pieces of polythene film were bombed separately so that corrections could be made for the energy released by their combustion. All analyses were carried out in duplicate. Gross energy values of diets, lactitol and freeze dried Duphalac were determined in triplicate or quadruplicate; N concentrations in the diets were also determined.

Calculations

Digestible energy value was calculated from the difference between gross energy values of the food consumed and the faeces collected, and it was expressed as kJ g^{-1} food. Metabolisable energy value was derived similarly, total excreta being considered rather than faeces alone. N-corrected metabolisable energy values were also calculated by correcting the energy balance by subtracting from it 28·33 kJ per g N retained in the case of the pig (Diggs *et al* 1965) and 26·33 kJ per g N retained in the case of the rat (Metta and Mitchell 1954).

From these values for the diets, energy values of lactitol and lactulose were calculated. For the pig, where test material was added to control starter diet, the following formula was used:

$$E = \frac{(1+i)E_c - E_c}{i}$$

where E is digestible (or metabolisable) energy value of test material (kJ g^{-1}); i is amount of test material added to 1 g of control diet (g); and E_e, E_c are digestible energy values of experimental and control diets, respectively (kJ g^{-1}).

In the rat experiment, the test materials replaced part of the maize starch in the control diet and so the following formula was appropriate:

$$E = E_s - \frac{E_c - E_e}{i}$$

where E_s is digestible (or metabolisable) energy value of maize starch (kJ g^{-1}); i is the concentration of test material in experimental diet (g g^{-1}); and E_e, E_c are as before. (Digestible energy value of maize starch is equal to its gross energy value of 17·48 kJ g^{-1} (Blaxter 1967); its metabolisable energy value is 16·58 kJ g^{-1}; Metta and Mitchell 1954.)

Statistical analysis

The data were subjected to standard analysis of variance for a cross-over experiment (Cochran and Cox 1957), and the standard errors of mean energy values for the diets are based on the residual error mean square with $r-2$ degrees of freedom where r is the number of animals. Each animal was its own control and generated an energy value for the test material. Mean values with standard errors for these energy values were also calculated.

RESULTS

In preliminary feeding trials with lactulose, rats showed a marked tendency to diarrhoea which made separation of faeces and urine impossible. For this reason, 75 g lactulose kg^{-1} diet was used for the experimental treatment as diarrhoea developed when the level of inclusion was 100 g kg^{-1}. A satisfactory adaptation to the experimental diet was achieved by feeding the rats a diet containing 50 g lactulose kg^{-1} for 2 days and then giving the experimental diet for 3 days before starting a balance. Lactulose was tolerated well by the pigs which consumed up to 310 g added to each kilogram of starter diet with few signs of diarrhoea. Lactitol was tolerated well by both pigs and rats, and an adaptation period was found unnecessary for the levels tested.

The results for individual animals in the nutritional balance studies are given in Tables 1–4 as the gross energy values of the food consumed and the excreta produced. The tables also give the digestible energy values and the metabolisable energy values, not corrected for nitrogen retention, derived from the intake and output data, and the corresponding values for lactitol and lactulose calculated from the energy values of the diets. Mean values with standard errors are given in Table 5. It should be noted that, by determination, the gross energy values of lactitol and lactulose were found to be 16·2 and 16·4 kJ g^{-1} respectively.

The experimental values for the diets were measured with high precision, as shown by coefficients of variation of 0·007–0·020, whereas for the derived values for the ingredients precision was of a lower order (coefficients of 0·12–0·38). This low

TABLE 1

Intake and excretion of gross energy (kJ day^{-1}) by growing miniature pigs fed on control diet and experimental diet containing lactitol, with digestible and metabolisable energy values (kJ g^{-1})

Pig number	*Diet*	*Energy intake*	*Faecal energy*	*Urinary energy*	*Digestible energy*		*Metabolisable energy*	
					Diet	*Lactitol*	*Diet*	*Lactitol*
19	Control	14001	2174	432	13·59	6·71	13·10	4·31
	Experimental	11582	2256	470	12·96		12·31	
21	Control	10525	1026	438	14·52	5·28	13·85	6·37
	Experimental	13495	2030	423	13·68		13·17	
23	Control	10525	1545	319	13·73	12·21	13·24	12·80
	Experimental	9563	1493	228	13·59		13·20	
25	Control	8690	1351	194	13·59	13·42	13·23	13·67
	Experimental	9563	1503	177	13·57		13·27	
27	Control	5214	788	115	13·66	9·02	13·31	9·24
	Experimental	5738	1020	106	13·24		12·94	
28	Control	6952	992	310	13·80	8·58	13·08	12·20
	Experimental	9563	1643	194	13·33		13·00	

TABLE 2

Intake and excretion of gross energy (kJ day^{-1}) by growing miniature pigs fed on control diet and experimental diet containing lactulose, with digestible and metabolisable energy values (kJ g^{-1})

Pig number	*Diet*	*Energy intake*	*Faecal energy*	*Urinary energy*	*Digestible energy*		*Metabolisable energy*	
					Diet	*Lactulose*	*Diet*	*Lactulose*
19	Control	9111	1125	222	14·10	8·53	13·71	6·87
	Experimental	8287	1213	310	13·26		12·68	
21	Control	7289	1115	255	13·62	12·34	13·06	11·57
	Experimental	10692	1494	403	13·29		12·70	
23	Control	7373	1125	325	13·63	7·90	12·92	8·29
	Experimental	8287	1402	294	12·90		12·35	
25	Control	5551	759	220	13·88	9·69	13·25	9·35
	Experimental	8620	1260	323	13·17		12·59	
27	Control	5635	980	254	13·29	6·67	12·56	6·92
	Experimental	6549	1355	236	12·20		11·65	
28	Control	5551	866	179	13·57	10·87	13·05	10·68
	Experimental	6882	1105	199	12·81		12·37	

TABLE 3

Intake and excretion of gross energy (kJ g^{-1}) by hooded rats fed on control diet and experimental diet containing lactitol, with digestible and metabolisable energy values (kJ g^{-1})

Rat number	*Diet*	*Energy intake*	*Faecal energy*	*Urinary energy*	*Digestible energy*		*Metabolisable energy*	
					Diet	*Lactitol*	*Diet*	*Lactitol*
1	Control	820·7	41·4	37·2	16·24	10·38	15·46	8·96
	Experimental	810·6	65·2	40·0	15·53		14·70	
2	Control	815·1	48·4	45·2	16·08	14·28	15·14	12·37
	Experimental	763·8	50·9	47·4	15·76		14·72	
3	Control	701·4	38·0	38·8	16·17	11·69	15·23	8·10
	Experimental	734·3	56·5	52·7	15·59		14·38	
4	Control	820·7	56·2	60·4	15·93	13·48	14·67	17·03
	Experimental	810·3	65·0	39·3	15·53		14·71	
5	Control	820·7	48·0	56·8	16·10	14·08	14·92	15·50
	Experimental	744·9	49·7	42·2	15·76		14·81	
6	Control	820·7	48·4	51·6	16·09	12·88	15·02	13·75
	Experimental	807·4	60·2	42·9	15·63		14·73	
7	Control	820·7	45·2	28·2	16·16	12·38	15·57	11·16
	Experimental	810·6	59·4	30·0	15·65		15·03	
8	Control	820·7	51·6	35·0	16·02	12·58	15·29	12·76
	Experimental	804·7	64·6	29·6	15·53		14·91	
9	Control	820·7	41·2	46·8	16·24	8·88	15·26	9·82
	Experimental	791·0	70·6	37·2	15·38		14·59	
10	Control	820·7	49·0	39·1	16·08	12·88	15·26	12·64
	Experimental	641·4	48·0	28·7	15·62		14·87	
11	Control	820·7	47·8	34·9	16·10	11·78	15·38	9·85
	Experimental	820·7	65·2	39·7	15·53		14·70	
12	Control	814·0	52·8	33·5	16·00	12·68	15·29	10·22
	Experimental	629·2	50·9	32·5	15·52		14·65	

TABLE 4

Intake and excretion of gross energy (kJ day^{-1}) by hooded rats fed on control diet and experimental diet containing lactulose, with digestible and metabolisable energy values (kJ g^{-1})

Rat number	*Diet*	*Energy intake*	*Faecal energy*	*Urinary energy*	*Digestible energy*		*Metabolisable energy*	
					Diet	*Lactulose*	*Diet*	*Lactulose*
1	Control	707·6	43·2	16·8	15·16	9·08	14·78	9·28
	Experimental	624·4	52·1	11·4	14·54		14·25	
2	Control	710·6	48·6	12·9	15·04	13·46	14·75	12·17
	Experimental	634·4	44·8	12·4	14·74		14·43	
3	Control	646·0	46·9	14·7	14·98	11·13	14·61	10·39
	Experimental	697·8	59·2	15·7	14·51		14·16	
4	Control	646·0	35·9	10·5	15·25	8·53	15·00	5·99
	Experimental	696·9	55·8	16·4	14·59		14·21	
5	Control	646·0	42·7	10·0	15·08	8·53	14·83	6·37
	Experimental	695·4	63·3	14·5	14·42		14·09	
6	Control	709·8	38·2	13·3	15·28	8·94	14·98	6·29
	Experimental	634·4	48·4	17·0	14·65		14·23	

TABLE 5

Energy values (kJ g^{-1}) of control and experimental diets determined with growing miniature pigs and hooded rats[a] and derived energy values of test materials, lactitol and lactulose

Test animal	*Test material*	*Energy value*	*Diet*			*Test material*	
			Control	*Experimental*	*SE*	*Mean*	*SE*
Miniature pig	Lactitol	Digestible	13·8	13·4	0·10	9·2	1·28
		Metabolisable	13·3	13·0	0·11	9·8	1·54
	Lactulose	Digestible	13·7	12·9	0·06	9·3	0·84
		Metabolisable	13·1	12·4	0·06	9·0	0·79
Hooded rat	Lactitol	Digestible	16·1	15·6	0·03	12·3	0·44
		Metabolisable	15·2	14·7	0·05	11·8	0·77
	Lactulose	Digestible	15·1	14·6	0·04	10·0	0·81
		Metabolisable	14·8	14·2	0·06	8·4	1·05

[a] Six animals per diet except that 12 rats were used for lactitol.

TABLE 6

Metabolisable energy values (kJ g^{-1}) of control and experimental diets corrected to zero N balance determined with growing miniature pigs and hooded rats[a] and derived energy values of test materials

Test animal	*Test material*	*Diet*			*Test material*	
		Control	*Experimental*	*SE*	*Mean*	*SE*
Miniature pig	Lactitol	12·9	12·6	0·11	10·0	1·52
	Lactulose	12·7	12·0	0·07	8·6	0·74
Hooded rat	Lactitol	15·1	14·6	0·04	11·6	0·61
	Lactulose	14·7	14·0	0·06	8·1	1·05

[a] Six animals per diet except that 12 rats were used for lactitol.

precision probably accounts for the unexpected result with pigs of a slightly higher value for the metabolisable energy of lactitol compared with its digestible energy value.

Table 6 shows metabolisable energy values corrected to zero N balance. Values for the diets were all slightly less than the uncorrected results (Table 5), more so in the pig than in the rat. The values derived for the test materials in Table 6 were little different from those obtained from the uncorrected energy values (Table 5), bearing in mind the lower precision.

DISCUSSION

The work described in this paper highlights one particular difficulty in the energy evaluation of poorly tolerated foodstuffs. The rats showed a tendency to diarrhoea when lactulose was tested, and to avoid this problem the levels of test materials were kept low. As a consequence the precision of the derived results was also low. This is because in the calculations (see pages 236 and 237) the level of inclusion is a divisor and, being small, it inflates the effect of any methodological or random errors. Further, there may be considerable animal-to-animal variation in the present experiments due to variation in the ability to digest and metabolise materials of the type tested. Any digestion probably depends on the activity of the gut flora within which there may be large differences between animals.

Although the amount of lactitol incorporated into the experimental diet was a rather small supplement for evaluation by the energy balance method, it is nevertheless representative of the amount that could be included in foods for man, and the results obtained here with rats and pigs may be applicable to the human. This remains to be fully investigated.

The reliability of the digestible and metabolisable energy values derived in this paper for lactitol and lactulose depends very much on the accuracy and precision of the gross energy values of the diet and excretory products which were determined by bomb calorimetry. As a check on this, the equation on page 237 for the rat results was used to calculate the gross energy values of lactitol and lactulose from the gross

energy values of the control and the respective experimental diets. This approach gave energy values (and SD) of 15·4 (1·4) kJ g^{-1} for lactitol and 11·1 (1·9) kJ ml^{-1} for Duphalac. These values compare with the determined values of 16·2 kJ g^{-1} and 12·5 kJ ml^{-1}, respectively. The calculated values are within 1 standard deviation of the determined ones, showing that the bomb calorimetry was reasonably accurate and precise. Such a check could not be applied to the determinations for pigs since their meals were prepared immediately before each feeding from appropriate quantities of control diet and test material.

The present results indicate that with lactitol considerable digestion of the test substance occurred and a similar picture emerged with lactulose. The ME values suggest that much of the digested energy was available for metabolic use by the pig or the rat. However, to ascertain the true extent of energy utilisation would require other experimental approaches. Product information supplied by the manufacturer of lactitol (CV Chemie Combinatie Amsterdam, CCA) gives a 'calorie utilisation' of lactitol in man of 8·4 kJ g^{-1} whereas in this work the metabolisable energy values of lactitol in rats and miniature pigs were found to be 11·8 and 9·8 kJ g^{-1} respectively. The energy value of lactitol was the subject of recent study in human volunteers (van Es *et al* 1986). In this report, an energy balance study indicated a metabolisable energy value of 80% of that of sucrose (saccharose). This is consistent with the data in this paper which indicate metabolisable energy values of 72 and 60% of gross energy values in the rat and miniature pig respectively.

Differences in energy values between man, rat and pig could be the result of differences in their gut microbial flora and its ability to break down lactitol. The porcine gut flora is in many respects similar to man's, but whereas the human stomach and upper small intestine are usually sterile, the stomach, duodenum and jejunum of pigs contain large numbers of bacteria. The most significant microbial activity in the porcine stomach is the fermentation of sugars, and this could represent an additional site for the digestion of lactitol in the pig. A difference between man and the rat that may be important is that the latter are known to practise coprophagy. Barnes *et al* (1957) estimated that even when rats are kept on wire mesh floors they recycle approximately 50% of their faeces. Despite considerable observation, particularly during the lengthy periods of time spent collecting the excreta, coprophagy was not seen during the experiments reported here, but it is nevertheless possible that a limited amount could have occurred.

Lactitol was originally proposed as a 'low-energy' sweetener and bulking agent with zero or nearly zero energy value. Investigations have shown that lactitol does contribute to the consumer's energy economy but there is insufficient data to be precise about the extent of this contribution. The ME values obtained in the present study suggest that lactitol may contribute too much energy to be of use in the manufacture of reduced-energy foods which in the UK must have no more than three-quarters of the energy value of the normal equivalent food. However, caution is required in drawing this conclusion since, as van Es *et al* (1986) proposed, the available energy may be considerably less than the ME value would suggest. Despite this uncertainty, lactitol does have certain other distinct characteristics which make it a useful ingredient for food technologists. The cariogenicity of lactitol is low (van der Hoeven 1986), so its use in products where it replaces sucrose may

contribute to a reduction in dental caries, particularly when it is used in the manufacture of chocolate, chewing gum, ice cream etc which are popular with children. Lactitol-containing foods may also be suitable for people suffering from diabetes, since the consumption of lactitol does not cause increased blood glucose or insulin levels (van Velthuijsen J A pers comm).

There do not appear to be any published energy values for lactulose in the literature. Its available energy has always been assumed to be small because it is not hydrolysed by homogenates of the human small intestinal mucosa (Dahlqvist and Gryboski 1965) and, on reaching the colon, it is metabolised by the bacteria to simple organic acids. The contribution these acids make to the energy balance of the host is a matter of continuing debate and investigation. However, the energy values reported here (8·4 and 9·0 kJ g^{-1} for the rat and pig respectively) suggest that the consumer may be able to derive more energy from lactulose than has been thought previously. This may be of interest to clinicians prescribing lactulose, particularly when it is used on a long-term basis to treat constipation in patients who may be bedridden or paraplegic and have problems limiting their energy intake.

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