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Conclusion from Canadian animal studies

Intake of dairy trans fatty acids protects against features of metabolic syndrome

Vaccenic acid, or 18:1 *trans*-11, is the most prevalent trans fatty acid (TFA) in ruminant milk and meat. The recently published 'Update on Trans Fatty acids' of the World Health Organization (1) showed that intake of TFA formed during industrial processing of vegetable oils is positively associated with risk of cardiovascular disease. The WHO experts concluded that no such association exists for intake of natural TFA such as vaccenic acid (2). During the congress of the International Dairy Federation in Berlin (2009), the Canadian researcher Dr Spencer Proctor (Alberta Institute for Human Nutrition, University of Alberta, Edmonton, Alberta, Canada) discussed indications that intake of vaccenic acid (VA) is even associated with reduced levels of risk factors for metabolic syndrome.

No human studies have been conducted to date of health effects of VA as such. There has been a study, however, in which healthy young men received butter enriched with VA and monounsaturated fatty acids from ruminant products (3). In another study, healthy young men followed a diet enriched with *cis*-9 *trans*-11 CLA (a VA conversion product formed in human metabolism) and VA (4). In other studies, postmenopausal women (5) and young men (6) were given a *cis*-9 *trans*-11 CLA-enriched diet. In those studies either a favourable effect (5) or a neutral effect (3, 4, 6) of the intervention diet on cardiovascular risk factors was found. Proctor reported that there are ongoing Canadian and American studies of the cardiovascular effect of VA intake in healthy women. Expectations are that results of those studies will be reported early in 2010.

Animal model for metabolic syndrome

Proctor: 'In Edmonton we have built up extensive experience with one of the best animal models for human metabolic syndrome, namely the JCR:LA-*corpulent phenotype* rat (7). Due to a mutation, that strain lacks activity of the leptin receptor on the plasma membrane. These animals develop spontaneously symptoms associated in man with metabolic syndrome and pre-diabetes including obesity, insulin resistance, hyperlipidaemia and inflammatory deregulation. In this excellently characterized animal model, we have conducted feeding studies with VA. My student Flora Wang, the first author of two recent publications on this subject (8, 9), received for these studies the Young Investigator Award during the International Symposium on Chylomicrons in Disease.'

	Gezonde ratten, controlevoer	Gezonde ratten, vacceenzuurvoer	Obese ratten, controlevoer	Obese ratten, vacceenzuurvoer
vacceenzuur	0.4±0.01	3.6±0.2*	0.4±0.02	1.0±0.3*
cis-9 trans-11 CLA	0.04±0.01	0.3±0.04*	0.04±0.02	0.3±0.01*

* Significantly different from the control feed (P<0.001).

Table 1. Effect of addition of vaccenic acid (VA) to the feed of healthy and corpulent phenotype rats for 3 weeks to incorporation of VA and cis-9 trans-11 CLA in triacylglycerol in adipose tissue. Figures stand for % of total fatty acids. Source: ref. 8.

Dietary vaccenic acid lowers cardiovascular risk

In the first study of Wang et al. (8), *corpulent phenotype* rats were administered for 3 weeks feed containing 43% carbohydrate, 28% protein and 15% fat with a polyunsaturated/saturated fatty acids (PUFA/SFA) ratio of 0.6 and an n-6/n-3 ratio of 10. In the feed of half of the animals 1.5% of the fat was replaced by VA at equal PUFA/SFA and n-6/n-3 ratios. These two feeds were also given to two control groups of rats with the normal phenotype ('healthy rats').

After three weeks feed consumption and weight gain were lower in healthy rats than in *corpulent phenotype* rats. Addition of VA to the feed did not change feed consumption or weight gain nor did it affect fasting glucose and insulin levels. Table 1 shows that addition to VA to the feed, for rats of both phenotypes, did result in greater incorporation of VA and *cis*-9 *trans*-11 CLA in triacylglycerol in adipose tissue.

Table 2 shows that VA supplementation led in *corpulent phenotype* rats, but not in healthy rats, to reduction in levels of cardiovascular risk factors, i.e. TAG (−35%), total cholesterol (−13%), LDL-cholesterol (−27%) and the inflammation markers interleukin-10 (IL-10, −66%) and haptoglobin (−20%). Proctor: 'In this short-term feeding study we see that VA in feed protects against features of metabolic syndrome - not in healthy animals but in animals with genetic predisposition for these features.'

	Healthy rats, control feed	Healthy rats, VA-enriched feed	Obese rats, control feed	Obese rats, VA-enriched feed
Triacylglycerol (mmol/l)	0.5±0,04	0.6±0.07	4.1±0.6	2.7±0.3*
Total cholesterol (mmol/l)	2.4±0.1	2.4±0.1	5.8±0.3	5.1±0.2*
LDL-cholesterol (mmol/l)	0.4±0.03	0.6±0.08	1.1±0.1	0.9±0.1*
IL-10 (nmol/l)	0.4±0.09	0.4±0.07	0.3±0.08	0,1±0.05*
Haptoglobin (pmol/l)	8.4±1.1	8.1±0.5	21.0±4.7	17.0±3.1

* Significantly different from the control feed (*P<0.01).

Table 2. Effect of addition of vaccenic acid (VA) to the feed of healthy rats and corpulent phenotype rats for 3 weeks on plasma level of lipids and serum levels of inflammation markers. Source: ref. 8.

Vaccenic acid intake reduces fatty degeneration of the liver

The second study (9) had a comparable design but a study duration of 16 weeks. In that study, again, the researchers found that addition of VA to the feed did not lead to deterioration of cardiovascular risk markers in healthy and *corpulent phenotype* rats. It was also confirmed that in *corpulent phenotype* rats addition of VA to feed improved blood lipids and inflammation markers. Serum TAG levels dropped by more than 50%, total cholesterol levels by 30% and LDL-cholesterol levels by 25%. Moreover, in *corpulent phenotype* rats dietary VA supplementation normalized the obesity-related raised haptoglobin level.

In rats, like in man, metabolic syndrome is associated with excess fat storage in the liver. Addition of VA to feed reduced fat deposition in the livers of *corpulent phenotype* rats by 60-70%. It also resulted in a modest decrease in levels of free fatty acids in the circulation. Besides, VA supplementation reduced liver activity of enzymes involved in hepatic fat synthesis. Figure 1 shows that addition to VA to the feed of *corpulent phenotype* rats led to a considerable decrease in activity of fatty acid synthase. 'That activity is not lowered to the level seen in healthy control rats but, metabolically, VA-supplemented rats still resemble healthy rats more than they do *corpulent phenotype* rats administered the control feed. That makes it likely that VA in the feed serves as a signal for the liver to store less fat.' In addition, there are indications for lowered postprandial fat absorption in VA-fed rats. Proctor: 'Figure 2 shows results of an oral fat challenge in rats at the end of the 16-week intervention. In rats on the control feed a much faster increase in plasma TAG levels was seen than in VA-fed rats. Moreover, we found that addition of VA to the feed of *corpulent phenotype* rats led to up-regulation of peroxisome proliferator-activated receptor á (PPAR-á) and PPAR-ã

in the intestine.'

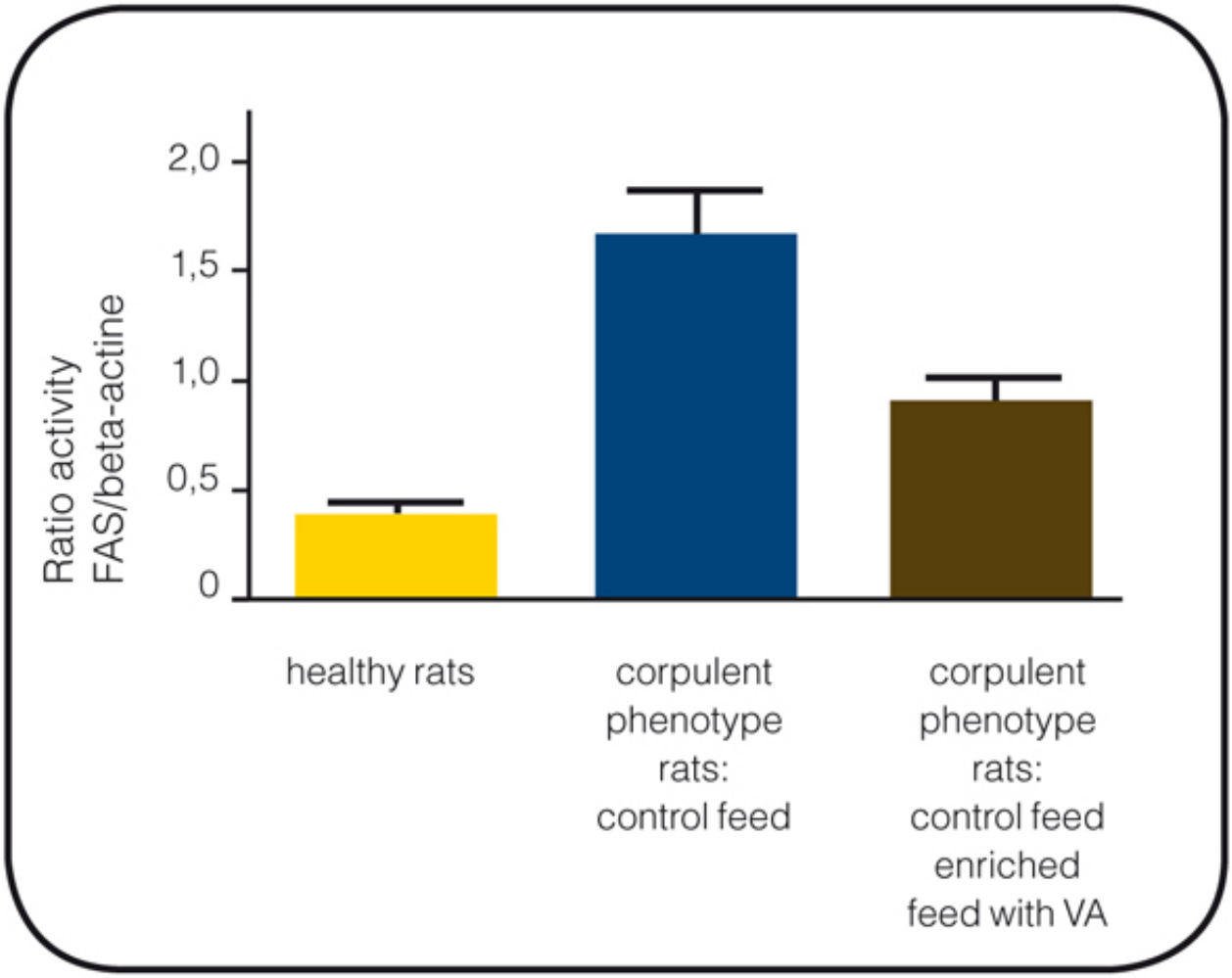

Figure 1. Effect of addition of vaccenic acid (VA) to the feed of healthy (lean) and corpulent phenotype (obese) rats for 16 weeks on fatty acid synthase (FAS) activity in liver. Differences between the three groups were significant (P<0.05). Source: ref. 9.

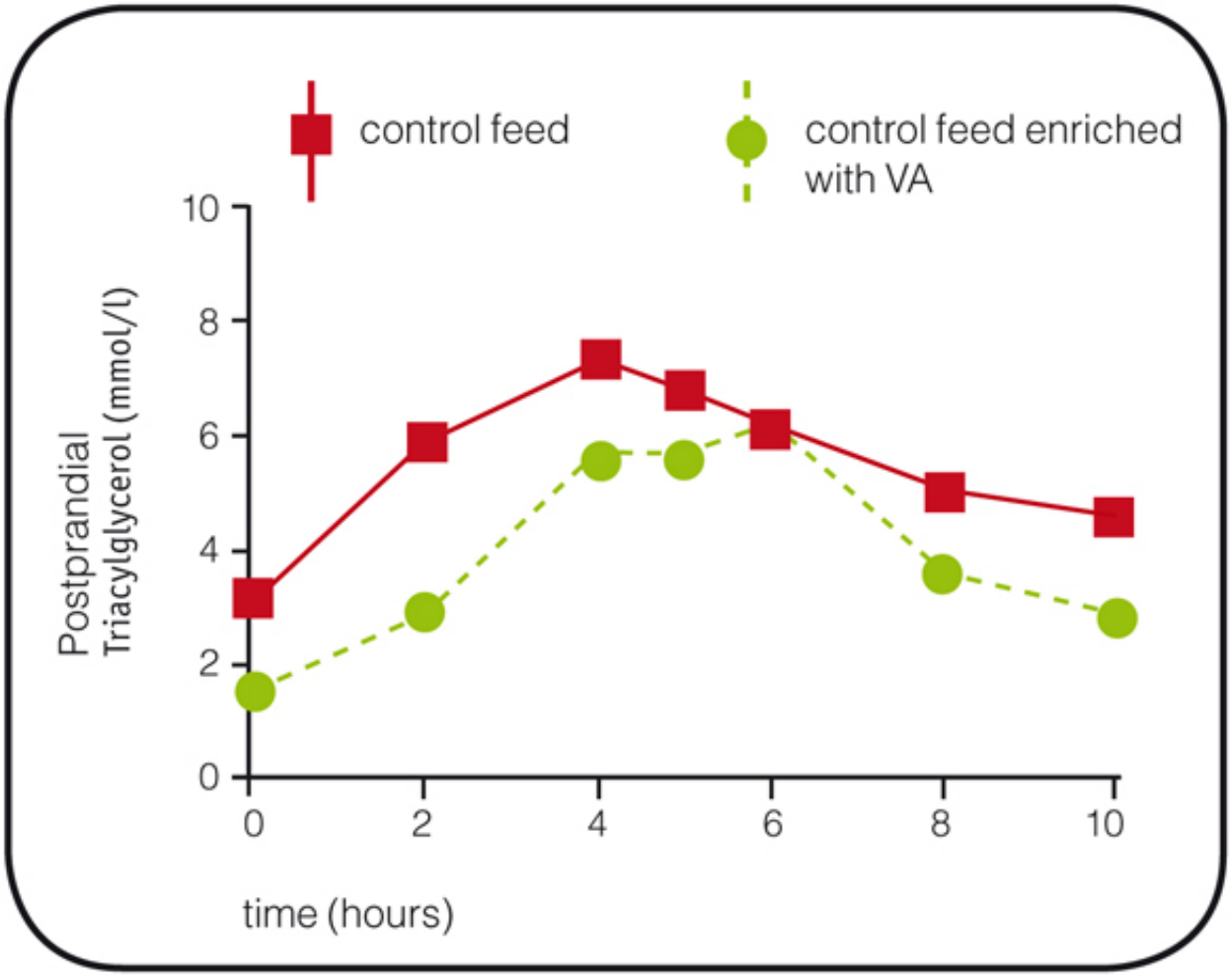

Figure 2. Postprandial response after an oral fat challenge of corpulent phenotype (obese) rats administered either a control feed or a control feed enriched with vaccenic acid (VA) for 4 months. Source: ref. 9.

In a pilot experiment with healthy and *corpulent phenotype* rats, Proctor and co-workers investigated the bioavailability of VA. They compared absorption of purified VA in a fat emulsion with absorption of VA from a food matrix. Absorption from food proved to be substantially higher for both rat types than absorption from a fat emulsion. In addition, rats with metabolic syndrome were found to absorb VA better than did healthy rats.

Distinction between natural and industrial trans fatty acids

It is not clear yet whether the effects of VA found are connected with conversion of VA into *cis*-9 *trans*-11 CLA or are independent of that. However, the answer to that question is not very relevant to nutritional practice. Proctor: 'I conclude, first of all, that addition of VA at a level of 1.6% of total energy intake to the feed of healthy as well as *corpulent phenotype* rats does not result in measurable deterioration of markers of cardiovascular health. Thus, in this

respect, dairy TFA distinguishes itself from industrial TFA. Furthermore, supplementation of VA to the feed of rats with metabolic syndrome leads to significant improvements in features of metabolic syndrome. We are currently seeking financial support for a comparable human study. It we could confirm our results in such a study, it would support distinction between natural and industrial TFA in nutritional recommendations.

References

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