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Ronald L. Prior
U.S. Meat Animal Research Center

Stephen B. Smith
U.S. Meat Animal Research Center

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Ronald L. Prior[1] and Stephen B. Smith

Summary

Rates of *in vitro* fat synthesis from acetate and lactate were compared to the activities of enzymes thought to be involved in the process of lipid synthesis from lactate. Results of these studies indicate that lactate can be incorporated into fats by a pathway heretofore thought to be nonfunctional in ruminants, the citrate cleavage:malic enzyme pathway. Studies of the effects of age and diet on the enzymes of the citrate cleavage:malic enzyme pathway support the concept of a physiological role for this pathway in lipid synthesis in beef cattle.

[1]Ronald L. Prior is a research chemist at MARC.

Introduction

Acetate, absorbed from the gastrointestinal tract of ruminants has historically been considered the only significant precursor for fat synthesis in the bovine animal. Recent studies in this and other laboratories, however, demonstrate that lactate can be converted to fats at appreciable rates in ruminant adipose tissue in the whole animal as well as in the laboratory. Lactate can either be absorbed from the gastrointestinal tract or produced by other tissues of the body for use by the adipose tissue. The only known route for converting lactate to fatty acids is the citrate cleavage:malic enzyme pathway. This pathway, however, has been considered to be nonfunctional in bovine adipose tissue because of the low activities of enzymes in the citrate cleavage:malic enzyme pathway relative to those observed in nonruminant adipose tissue.

We designed initial experiments to determine whether or not key enzymes in the citrate cleavage:malic enzyme pathway had enough activity to support rates of lipid synthesis from lactate observed in the laboratory. Subsequently, studies were undertaken to determine if age and diet could affect the activities of these enzymes.

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Table 1.—Composition of pelleted diets[1]

Ingredient	Ration 1 (roughage)	Ration 2 (high concentrate)
Ground alfalfa hay	100	9.71
Ground corn	---	78.69
Soybean meal	---	5.05
Calcium chloride	---	1.10
Trace mineralized salt	---	.45
Binder (lignin sulfate)	---	5.00
Vitamins ADE[2]	---	+
		100.00

[1]Percent on as fed basis.
[2]Added to provide 22,000 IU A, 2,200 IU D, and 220 IU E per lb diet.

Experimental Procedure

Experiment 1. Samples of subcutaneous adipose tissue (backfat) were obtained by biopsy technique from Angus-Hereford crossbred finishing steers (1063 ± 31 lb) fed a high-energy ration. We then analyzed samples for the rate of fat synthesis from either acetate or lactate. A portion of each biopsy sample was homogenized, and crude centrifugal fractions of the homogenates were used for the analysis of enzyme activities.

Experiment 2. Twenty Angus-Hereford and Red Poll steers were divided into two groups of 10 animals each. Both groups were initially fed a ration consisting of pelleted sun-cured alfalfa hay. When the steers were approximately 250 days of age, one group was gradually switched to a pelleted high concentrate diet (Table 1). Biopsy samples of subcutaneous fat were obtained every 35 to 70 days, homogenized, and analyzed for enzyme activities.

Table 2.—Acetate and lactate incorporated into fatty acids in bovine subcutaneous adipose tissue

Substrates[1]	Incorporation rates (nmol/min per g adipose tissue)
10 mM Acetate	8.2 ± 2.5
plus 2mM Glucose	30.2 ± 6.3
10 mM Lactate	33.3 ± 6.5
plus 2 mM Glucose	47.5 ± 6.3

[1]Flasks that contained glucose also contained 33 mu/ml of insulin.

Results

Experiment 1. Rates of incorporation of acetate and lactate into fatty acids are listed in Table 2. Even though acetate is thought to be the major precursor for lipid synthesis in beef cattle, we incorporated lactate into fats at rates that exceeded those from acetate in both the absence and presence of glucose. Our research shows that lactate might be an important substrate for fat synthesis in whole animals.

Citrate cleavage enzyme, malic enzyme, and pyruvate carboxylase activities are listed in Table 3. The activities of the enzymes, all of which are involved in the citrate cleavage:malic enzyme pathway, are about one-tenth of the activities observed in nonruminant adipose tissue. All three enzymes, however, exhibit sufficient activity to account for the rates of lipid synthesis from lactate (Table 2).

Furthermore, the activities of citrate cleavage enzyme, malic enzyme, and pyruvate carboxylase are equal to or exceed that of acetyl-CoA carboxylase. Acetyl-CoA carboxylase has been shown to be involved in lipid synthesis from acetate and presumably is required for lipid synthesis from lactate. Therefore, the citrate cleavage:malic enzyme pathway should not be considered nonfunctional merely because key enzymes in this pathway are low in the adipose tissue of beef animals relative to those in nonruminants.

Experiment 2. As is typically observed, steers fed the high-concentrate diet grew at a faster rate than those on the alfalfa hay ration (Table 4). The activities of acetyl-CoA carboxylase, citrate cleavage enzyme, and malic enzyme were extremely low at the first biopsy. Enzyme activities increased gradually until the steers were 420 days old. Between 420 and 489 days of age, the activities of acetyl-CoA carboxylase and citrate cleavage enzyme abruptly increased two- to fourfold in the alfalfa hay-fed steers and eight- to tenfold in the high concentrate-fed steers. Enzyme activities declined significantly after 540 days of age. Malic enzyme activity doubled in the alfalfa hay-fed steers and tripled in the high concentrate-fed steers between 315 and 350 days of age. After 420 days of age, malic enzyme activity remained constant in the alfalfa hay-fed steers but had doubled in the high concentrate-fed steers by 489 days of age. The data indicate that the activities of lipogenic enzymes are not influenced by diet in beef cattle until the animals reach a specific age, corresponding to the time at which enzyme activities are increasing independently of dietary regime. Furthermore, citrate cleavage enzyme and malic enzyme responded to changes in age and diet in the same manner as acetyl-CoA carboxylase, supporting the concept of functional, biologically important, citrate cleavage:malic enzyme pathway.

Table 3.—Lipogenic enzyme activities in bovine subcutaneous adipose tissue

Enzyme	Maximal activity (nmol/min/g adipose tissue)
Citrate cleavage enzyme	78.8 ± 10.1
Malic enzyme	207.4 ± 23.5
Pyruvate carboxylase	42.4 ± 4.9
Acetyl-CoA carboxylase	54.0 ± 15.8

Table 4.—Effect of age and diet on lipogenic enzyme activities

Treatment group	Average age (days)	Weight (lb)	Enzyme activities (nmol/min/g adipose tissue)		
			AcCoA carboxylase	Citrate cleavage enzyme	Malic enzyme
		(lb)			
I	280	575 ± 16	1.8 ± 0.9	2.6 ± 0.7	21.9 ± 1.9
II		534 ± 13	1.9 ± 1.1	1.9 ± .7	21.1 ± 3.4
I	315	640 ± 19	4.7 ± 1.9	1.8 ± .2	31.5 ± 4.3
II		595 ± 12	8.9 ± 2.2	2.3 ± .3	29.3 ± 4.4
I	350	704 ± 23	8.0 ± 1.3	6.7 ± .7	61.1 ± 6.5
II		667 ± 14	18.4 ± 4.0	15.9 ± 4.9	98.9 ± 19.2
I	420	818 ± 27	22.8 ± 5.3	12.0 ± 2.4	91.5 ± 19.3
II		813 ± 22	16.0 ± 4.6	18.7 ± 5.2	107.4 ± 22.2
I	490	928 ± 28	48.5 ± 13.6	45.6 ± 13.5	81.1 ± 19.7
II		964 ± 32	129.1 ± 47.9	[1]197.9 ± 44.2	[1]181.1 ± 29.8
I	542	1023 ± 28	73.9 ± 16.6	47.8 ± 13.3	105.7 ± 15.7
II		1080 ± 40	[1]156.0 ± 21.1	[1]149.6 ± 36.7	[1]214.9 ± 23.8
I	574	1084 ± 30	65.1 ± 8.6	28.5 ± 7.3	80.2 ± 11.4
II		1150 ± 44	[1]95.7 ± 10.9	[1]90.1 ± 8.3	[1]233.0 ± 24.2

[1]Significantly greater than Treatment I value ($P<0.05$; Student's t-test).