Interleukin-1 and lipid metabolism in the rat

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Intravenous administration of a single dose (20 µg) of recombinant interleukin-1-β to virgin, lactating and litter-removed rats rapidly decreased intestinal lipid absorption in all groups. *In vivo*, oxidation of [¹⁴C]triolein to ¹⁴CO₂ was also significantly decreased by interleukin-1. In addition, the cytokine decreased [¹⁴C]lipid accumulation in the mammary gland of lactating rats and in the adipose tissue of virgin and litter-removed rats. The decrease in lipid uptake in the interleukin-treated rats was accompanied by hypertriglyceridaemia; however, there was no significant decrease in tissue lipoprotein lipase activity, except in heart from lactating rats. In contrast, interleukin-1 administration had no effect on lipogenesis in liver, white or brown adipose tissue of virgin rats fed on glucose. These results suggest that interleukin-1 profoundly affects lipid metabolism by delaying intestinal absorption and decreasing tissue uptake.

INTRODUCTION

Interleukin-1, primarily produced from phagocytic cells, is a polypeptide capable of mediating the host's responses to infection and inflammation (see Dinarello, 1984). The physiological and metabolic effects that follow interleukin-1 administration to experimental animals are varied and include fever (Dinarello & Wolff, 1982), neutrophil activation (Kampschmidt, 1984), B- and T-cell activation (Falkoff *et al.*, 1983; Mizel, 1982), enhanced liver protein synthesis (Pepys & Baltz, 1983) and amino acid release from skeletal muscle (Baracos *et al.*, 1983). Studies *in vitro* have also shown the ability of interleukin-1 to decrease lipoprotein lipase activity in cultured 3T3-L1 adipocytes by inhibiting the synthesis of the enzyme (Price *et al.*, 1986). Little is known of the effects of interleukin-1 *in vivo* on lipid metabolism. We have therefore studied the effects of acute interleukin-1 administration on the utilization of dietary lipid ([¹⁴C]triolein) in virgin, lactating and litter-removed rats. Lactation was chosen as a model because it involves important changes in partitioning of dietary fat between mammary gland and adipose tissue (see Williamson, 1980; Vernon & Flint, 1983; Scow & Chernick, 1987). Lactation decreases lipogenesis (Agius *et al.*, 1979), lipoprotein lipase (Hamosh *et al.*, 1970; Flint *et al.*, 1981) and lipid uptake (Oller do Nascimento & Williamson, 1986) in adipose tissue, but enhances metabolic activity in the mammary gland (Williamson, 1986). The lactating mammary gland has increased rates of lipogenesis, increased lipoprotein lipase activity and lipid uptake. These tissue-specific changes in lipid metabolism are rapidly reversed on removal of the suckling litter (Williamson, 1980; Vernon & Flint, 1983; Oller do Nascimento & Williamson, 1986; Scow & Chernick, 1987).

EXPERIMENTAL

Animals

Female Wistar rats were fed *ad libitum* on a chow diet consisting of (by wt.) 52% carbohydrate, 21% protein

and 4% fat (the residue was non-digestible material; Special Diet Services, Witham, Essex, U.K.) with free access to drinking water, and were maintained at an ambient temperature of 22 ± 2 °C with a 12 h-light/12 h-dark cycle (lights on from 07:00 h). Three groups of rats were studied: Group 1 were virgin females (212 ± 5.0 g), Group 2 were lactating rats (285 ± 15 g) with eight to eleven pups used 10–13 days *post partum*, and Group 3 were lactating rats (315 ± 10 g) whose litters had been prematurely removed for 24 h, 10–13 days *post partum*.

Biochemicals

All enzymes and coenzymes were purchased from Boehringer Corp. (London) Ltd., Lewes, Sussex, U.K. [¹⁴C]Triolein (glycerol tri[¹⁴C]oleate) and glycerol tri[9,10(n)-³H]oleate were obtained from Amersham International, Amersham, Bucks., U.K. Human recombinant interleukin-1-β was kindly given by Eli Lilly and Co., Indianapolis, IN, U.S.A.

Measurement of lipid oxidation and tissue lipid accumulation

At 1 h after the intravenous administration (tail vein) of a single dose of interleukin-1-β (20 µg in 0.5 ml of 0.9% NaCl) or saline, the metabolic fate of an orally administered [¹⁴C]lipid load was examined as described by Oller do Nascimento & Williamson (1986). About 0.5 g (0.82 µCi) of [¹⁴C]triolein per rat was given enterally by gastric intubation, without anaesthetic but with minimal stress to the animal. Expired CO₂ was then collected hourly for 5 h by absorption in Lumasorb (May & Baker, Dagenham, Essex, U.K.), and the rate of ¹⁴CO₂ production was estimated by counting radioactivity in a sample of the Lumasorb. After the 5 h collection period, the animal was killed. Arterial blood was collected in a heparinized syringe. The gastrointestinal tract (plus contents) was homogenized in 150 ml of 3% (w/v) HClO₄. Duplicate samples were taken of liver, perigenital and perirenal white adipose tissue, mammary gland and interscapular brown adipose tissue (single sample). Carcass (minus liver, mammary

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gland and intestinal tract) was treated as previously described (Oller do Nascimento & Williamson, 1988). Tissues were saponified and the lipid was extracted (Stansbie *et al.*, 1976). The amount of lipid extracted from the carcass was determined gravimetrically. The extracted fatty acids were dissolved in 10 ml of scintillation fluid (Optiphase 'Safe'; LKB) for measurement of radioactivity and hence determination of [^{14}C]lipid accumulation. [1- ^{14}C]Triolein absorption was calculated by subtracting total gastrointestinal radioactivity from that administered.

Lipoprotein lipase

Perigenital-adipose-tissue, heart and mammary-gland lipoprotein lipase activities were estimated by a modification of the technique of Nilsson-Ehle & Ekman (1977). Tissue samples were dried to a powder with acetone/diethyl ether, and then resolubilized and used in an assay system containing [^3H]triolein as substrate; ^3H -labelled fatty acids released after a 60 min incubation period were extracted and determined by the method of Nilsson-Ehle & Schotz (1976). Lipoprotein lipase activity is expressed as nmol of fatty acid released/min per mg of acetone-dried powder. Post-heparin plasma lipolytic activity was measured in control and interleukin-treated virgin rats 20 min after intravenous injection (femoral vein) of 1000 units of heparin/kg body wt., in accordance with the procedure of Kuwajima *et al.* (1988).

Measurement of lipogenesis

Lipogenesis *in vivo* was determined 5 h after the administration of either saline or interleukin-1. An intragastric glucose (4 mmol) load to stimulate lipogenesis (Agius & Williamson, 1980) was given 90 min before death of the rat. Lipogenic rate *in vivo* was determined with $^3\text{H}_2\text{O}$ as previously described (Robinson *et al.*, 1978). At 1 h before being killed, animals were injected with 0.3 ml (3.0 mCi) of $^3\text{H}_2\text{O}$ intraperitoneally; 5 min before death the animals were anaesthetized with pentobarbital (60 mg/kg body wt.). Tissues were saponified and fatty acids extracted by the method of Stansbie *et al.* (1976). The amount of glucose load absorbed was measured as described by Mercer & Williamson (1987).

Blood metabolites and plasma insulin

Whole-blood glucose was determined by the method of Slein (1963) and lactate by the method of Hohorst (1963). Plasma triacylglycerol was measured by the method of Eggstein & Kreutz (1966). Plasma glycerol was measured by the method of Garland & Randle (1962), and plasma non-esterified fatty acids were measured with an enzymic colorimetric method (Wako Chemicals G.m.b.H, Neuss, West Germany). Plasma insulin was determined by radioimmunoassay with a rat insulin standard (Albano *et al.*, 1972).

RESULTS AND DISCUSSION

Absorption, oxidation and tissue accumulation of an oral [^{14}C]triolein load

Treatment with interleukin-1 decreased (by 40–50 %) intestinal absorption of lipid in all the experimental groups (Table 1). Results of [1- ^{14}C]triolein disposal have therefore been expressed as % of absorbed dose.

Administration of interleukin-1 decreased oxidation

of [^{14}C]lipid to $^{14}\text{CO}_2$ (2–3-fold), over a 5 h period, in all groups (Table 1). As expected, $^{14}\text{CO}_2$ production was higher in the control virgin than in the control lactating and litter-removed rats (Table 1; Oller do Nascimento & Williamson, 1986).

Interleukin-1 treatment decreased lipid accumulation in most of the tissues studied (Table 1); however, the effects differed between tissues and between the experimental groups. In both virgin and litter-removed rats, [^{14}C]lipid accumulation was significantly decreased in carcass and adipose tissue (white and brown) in the interleukin-1-treated group. In contrast, lactating rats showed a marked decrease of [^{14}C]triolein deposition in mammary gland, with no significant changes in [^{14}C]lipid accumulation in carcass or adipose tissue (brown or white) (Table 1). Pup lipid accumulation was also significantly decreased by interleukin-1. It seems that this cytokine can affect lactation via inhibition of the uptake of circulating dietary lipid by mammary gland. Interleukin-1 treatment increased the accumulation of saponified [^{14}C]lipid in the liver of the litter-removed group. Accumulation in the non-saponified (sterol) lipids was low and not altered by interleukin-1. The overall effect of interleukin-1 on dietary lipid disposal is particularly marked if total mammary-gland and adipose-tissue accumulation are estimated (Table 1). In lactating rats, interleukin-1 caused a significant decrease (45 %) in total mammary-gland accumulation, whereas in litter-removed rats, the effect of the cytokine was on adipose tissue (70 % decrease) (Table 1).

Gastrointestinal partitioning of the [^{14}C]lipid

To see if the striking effects of interleukin-1 on intestinal lipid absorption were related to altered gastrointestinal transit, the distribution of the [^{14}C]triolein between the stomach and the intestine was studied (Table 2). In all control groups, 5 h after the administration of the tracer, most of the residual label (60–80 %) was already in the intestine, having left the stomach. Interleukin-1 reversed this pattern of distribution: most of the label was found in the stomach (58–70 %) of the treated animals. Similar results were found when the gastric and intestinal contents of glucose and lactate were measured after an oral load of glucose (4 mmol) to virgin rats. Absorption of glucose from the intestinal tract was decreased from 74.3 ± 5.9 (control group; $n = 5$) to 40.2 ± 3.9 (treated group; $n = 5$). The distribution of glucose and lactate in the gastrointestinal tract was affected by interleukin-1 in a similar way to that of triolein (J. M. Argilés & F. J. Lopez-Soriano, unpublished work). It seems probable that the action of the cytokine upon absorption is to slow gastric transit, which, in turn, significantly affects nutrient uptake. Others have shown that another cytokine, tumour necrosis factor, inhibits gastric emptying (Patton *et al.*, 1987), but as far as we are aware this has not been reported for interleukin-1.

Lipoprotein lipase and plasma triacylglycerols

To examine whether the decreased tissue accumulation of dietary [^{14}C]lipid after interleukin-1 treatment was due to a decrease of lipoprotein lipase activity, the enzyme responsible for the hydrolysis of plasma triacylglycerols (see Robinson, 1970), the activity was measured in white adipose tissue, mammary gland and heart (Table 3). Although there was a tendency for interleukin-1 to

Table 1. Effects of interleukin-1 on the absorption and metabolic fate of orally administered [1-¹⁴C]triolein in fed virgin, lactating and litter-removed rats

For full details see the Experimental section. ¹⁴CO₂ production was calculated during the course of the 5 h after triolein administration. The results are mean values ± S.E.M. for five observations. Total estimated adipose-tissue accumulation was calculated assuming that all carcass fat corresponded to adipose tissue. Interleukin-1-treated values that are significantly different by Student's *t* test from their corresponding control values are indicated by: **P* < 0.05, ***P* < 0.01, ****P* < 0.001.

Measurement	Treatment	State of rats		
		Virgin	Lactating	Litter-removed
Absorption (% of administered dose)	Control	76.5 ± 2.2	82.1 ± 4.8	83.0 ± 1.8
	Interleukin-1	31.8 ± 4.0***	36.3 ± 1.2***	41.8 ± 4.9***
¹⁴ CO ₂ production (% of absorbed dose)	Control	33.4 ± 4.15	13.1 ± 2.62	10.0 ± 1.70
	Interleukin-1	10.8 ± 3.07**	4.64 ± 1.07*	6.38 ± 0.72*
Tissue accumulation (% of absorbed dose/g)				
Carcass (mother)	Control	0.17 ± 0.02	0.04 ± 0.01	0.24 ± 0.01
	Interleukin-1	0.08 ± 0.02*	0.08 ± 0.03	0.12 ± 0.01***
Carcass (pups)	Control	—	0.06 ± 0.02	—
	Interleukin-1	—	0.01 ± 0.003*	—
Liver (saponified)	Control	0.63 ± 0.05	0.23 ± 0.06	0.47 ± 0.03
	Interleukin-1	0.47 ± 0.12	0.34 ± 0.06	0.69 ± 0.05**
Liver (non-saponified)	Control	0.06 ± 0.006	0.03 ± 0.006	0.06 ± 0.01
	Interleukin-1	0.04 ± 0.009	0.03 ± 0.006	0.06 ± 0.006
Mammary gland	Control	—	2.32 ± 0.12	0.10 ± 0.01
	Interleukin-1	—	1.34 ± 0.14***	0.08 ± 0.02
Brown adipose tissue	Control	5.59 ± 1.46	0.20 ± 0.09	4.33 ± 0.85
	Interleukin-1	1.88 ± 0.58*	0.17 ± 0.06	1.47 ± 0.36*
Perirenal white adipose tissue	Control	0.71 ± 0.18	0.04 ± 0.006	2.41 ± 0.52
	Interleukin-1	0.12 ± 0.03*	0.05 ± 0.01	0.74 ± 0.08*
Perigenital white adipose tissue	Control	0.62 ± 0.16	0.03 ± 0.007	1.96 ± 0.35
	Interleukin-1	0.14 ± 0.04*	0.04 ± 0.009	0.87 ± 0.23*
Plasma	Control	0.08 ± 0.005	0.07 ± 0.01	0.12 ± 0.01
	Interleukin-1	0.14 ± 0.03	0.17 ± 0.04*	0.70 ± 0.18*
Total estimated white-adipose-tissue accumulation	Control	17.4 ± 5.97	0.53 ± 0.14	46.2 ± 7.19
	Interleukin-1	3.8 ± 1.26	0.56 ± 0.14	13.4 ± 2.05**
Total estimated mammary-gland accumulation	Control	—	37.6 ± 3.21	2.9 ± 0.57
	Interleukin-1	—	20.8 ± 1.87**	2.2 ± 0.26

Table 2. Effects of interleukin-1 on the distribution of [1-¹⁴C]triolein in the gastrointestinal tract of virgin, lactating and litter-removed rats

Deproteinized samples of stomach and intestine of the different groups of rats, 5 h after the administration of the tracer, were used to assess partition of the residual lipid fraction. The results, expressed as % of total residual lipid, are mean values of two or three rats in each group. For full details see the Experimental section.

Tissue	State of rats					
	Virgin		Lactating		Litter-removed	
	Control	Interleukin-1	Control	Interleukin-1	Control	Interleukin-1
Stomach	19.9	64.7	20.2	58.6	39.3	69.2
Intestine	80.1	35.3	79.8	41.4	60.7	30.8

decrease the activity in white adipose tissue of virgin and litter-removed rats and lactating mammary gland, the changes are not significant. The only significant decrease was in heart of the lactating group. This lack of effect of interleukin-1 on lipoprotein lipase activity in the present experiments is in contrast with the pronounced inhibition

in 3T3 L1 adipocytes *in vitro* (Price *et al.*, 1986). Despite this, there was marked hypertriglyceridaemia in all interleukin-treated groups (Table 3). Thus the decreased lipid accumulation in the tissues, together with the increased plasma triacylglycerol, is evidence of impairment of functional lipoprotein lipase activity, although

Table 3. Effects of interleukin-1 on plasma triacylglycerol, glycerol and non-esterified fatty acid concentrations and tissue lipoprotein lipase activity in fed virgin, lactating and litter-removed rats

For full details see the Experimental section. The results are mean values $\pm$ S.E.M. for five observations except where otherwise stated. Lipoprotein lipase activity is expressed as nmol of fatty acid released/min per mg of acetone-dried powder. Values that are significantly different by Student's *t* test from control values are indicated by: **P* < 0.05, ***P* < 0.01, ****P* < 0.001.

Measurement	Treatment	State of rats		
		Virgin	Lactating	Litter-removed
Lipoprotein lipase activity White adipose tissue	Control	1.150 $\pm$ 0.172	0.301 $\pm$ 0.041	0.985 $\pm$ 0.138
	Interleukin-1	0.704 $\pm$ 0.199	0.260 $\pm$ 0.025	0.795 $\pm$ 0.105
Mammary gland	Control	—	0.524 $\pm$ 0.102	0.032 $\pm$ 0.006
	Interleukin-1	—	0.306 $\pm$ 0.037	0.032 $\pm$ 0.014
Heart	Control	0.437 $\pm$ 0.056	0.340 $\pm$ 0.080	0.219 $\pm$ 0.074
	Interleukin-1	0.385 $\pm$ 0.041	0.137 $\pm$ 0.022*	0.180 $\pm$ 0.043
Plasma triacylglycerol (mg/100 ml)	Control	51.9 $\pm$ 3.5	62.1 $\pm$ 6.7	176.6 $\pm$ 32.8
	Interleukin-1	99.2 $\pm$ 14.0**	264.4 $\pm$ 32.2***	801.5 $\pm$ 163.5*
Plasma glycerol (nmol/ml)	Control	168 $\pm$ 13 (4)	172 $\pm$ 37 (4)	292 $\pm$ 58 (3)
	Interleukin-1	228 $\pm$ 25 (4)	212 $\pm$ 25 (3)	235; 452 (2)
Plasma non-esterified fatty acids (nequiv./ml)	Control	552 $\pm$ 60	711 $\pm$ 139 (4)	1390 $\pm$ 276 (4)
	Interleukin-1	816 $\pm$ 113	934 $\pm$ 117	2626 $\pm$ 395 (4)*

the hypertriglyceridaemia may also in part be due to increased adipose tissue lipolysis as occurs in 3T3 L1 adipocytes (Price *et al.*, 1986) and subsequent increased secretion of very-low-density lipoproteins from the liver. Further support for these views is that plasma post-heparin lipolytic activity, an index of heparin-releasable lipases, was significantly decreased (*P* < 0.05) in interleukin-treated virgin rats [341 $\pm$ 66 (4) nmol of fatty acid released/min per ml of plasma, versus 523 $\pm$ 10 (4) for control virgin rats]. Despite this evidence for impairment of functional lipoprotein lipase activity, plasma glycerol and plasma non-esterified fatty acids were not decreased by interleukin treatment (Table 3) and tended to be higher than the control values. As the two major potential sources of plasma glycerol and non-esterified fatty acids are the activities of lipoprotein lipase or hormone-sensitive triacylglycerol lipase in adipose tissue, the present evidence supports the view that there is increased lipolysis in adipose tissue in interleukin-treated rats.

Tissue lipogenesis *in vivo*

Interleukin-1 has no acute effect on the synthesis of fatty acids *de novo* as measured by [¹⁴C]acetate incorporation into lipid in 3T3 L1 adipocytes (Price *et al.*, 1986). To examine whether this is true *in vivo*, the lipogenic rate was measured with ³H₂O in white and brown adipose tissues, liver and carcass of virgin rats after interleukin-1 administration and oral glucose. There were no significant differences in the lipogenic rate of these tissues between the control and interleukin-1-treated animals (Table 4). Lipogenesis was not measured in the lactating group, because food availability modulates mammary-gland lipogenesis (Williamson *et al.*, 1983) and the decreased intestinal absorption observed after interleukin-1 treatment might influence the lipogenic rate of the mammary tissue *in vivo* (Mercer

Table 4. Effects of interleukin-1 on tissue lipogenesis in virgin rats

The results are mean values $\pm$ S.E.M. for five rats in each group, expressed as μ mol of ³H₂O incorporated into saponified lipid/h per g wet wt. of tissue. For further details see the Experimental section.

Tissue	Rate of lipogenesis (μ mol/h per g)	
	Control	Interleukin-1
Carcass	3.19 $\pm$ 0.44	3.53 $\pm$ 0.38
Liver	17.3 $\pm$ 5.1	19.9 $\pm$ 5.3
White adipose tissue	8.40 $\pm$ 3.4	6.82 $\pm$ 1.1
Brown adipose tissue	105.3 $\pm$ 24.1	90.2 $\pm$ 31.2

& Williamson, 1987) and be confused with an effect of the cytokine.

Blood metabolites and plasma insulin

Interleukin-1 administration caused a tendency to hypoglycaemia in all experimental groups, but this was only significant in the lactating group (Table 5). Blood lactate concentrations were not altered by interleukin-1 treatment. Interleukin-1 tended to increase plasma insulin concentrations, leading to an increase in the insulin/glucose ratio, but this was only significant in the virgin group. The effects *in vitro* of interleukin-1 on insulin secretion from isolated rat pancreatic islets are variable, both inhibition and stimulation occurring depending on the experimental conditions (Comens *et al.*, 1987). The maintenance plasma insulin in the interleukin-1-treated rats suggests that changes in the concentration of the

Table 5. Effects of interleukin-1 on blood glucose and lactate, and on plasma insulin in fed, virgin, lactating and litter-removed rats

For full details see the Experimental section. The results are mean values $\pm$ S.E.M. for five rats, expressed as $\mu\text{mol}/\text{ml}$ of blood. For the calculation of insulin/glucose ratios, insulin was expressed as $\mu\text{units}/\text{ml}$ of plasma. Values that are significantly different by Student's *t* test from control values are indicated by **P* < 0.05, ****P* < 0.001.

State of rats	Blood metabolite ($\mu\text{mol}/\text{ml}$)		Insulin/ glucose ratio
	Glucose	Lactate	
Virgin			
Control	6.75 $\pm$ 0.38	2.21 $\pm$ 0.12	5.1 $\pm$ 0.9
Interleukin-1	5.55 $\pm$ 0.55	2.75 $\pm$ 0.42	11.6 $\pm$ 2.9*
Lactating			
Control	5.50 $\pm$ 0.14	3.51 $\pm$ 0.65	2.0 $\pm$ 0.3
Interleukin-1	4.33 $\pm$ 0.11***	3.96 $\pm$ 0.68	3.2 $\pm$ 0.5
Litter-removed			
Control	6.20 $\pm$ 0.41	4.03 $\pm$ 0.31	8.8 $\pm$ 2.4
Interleukin-1	5.00 $\pm$ 0.35	3.50 $\pm$ 0.26	11.0 $\pm$ 2.0

hormone are not involved in the alterations in tissue lipid accumulation (see Oller do Nascimento & Williamson, 1988).

Comparison of effects of interleukin-1, tumour necrosis factor- α and tumour growth

The present results and those of previous studies from this laboratory (Evans & Williamson, 1988a,b) allow a comparison to be made of the effects *in vivo* on lipid metabolism of the two related cytokines, interleukin-1 and tumour necrosis factor- α (cachectin), and of tumour growth (Table 6). However, such comparisons must be viewed with some caution, because the dose of tumour necrosis factor was approx. 8-fold higher than that of interleukin-1, and the cytokines were only studied in the acute situation, whereas tumour burden was present for 8–10 days. The two cytokines had very similar effects on lipid metabolism, including decreased absorption, decreased oxidation, decreased deposition in white and brown adipose tissue and lactating mammary gland of an oral lipid load, and hypertriglyceridaemia. The major difference was that there was no significant decrease in measured lipoprotein lipase activity in interleukin-1-treated rats, although the effects on lipid metabolism of the cytokine suggested an impairment of the functional enzyme activity. The similarity of the effects of interleukin-1 and tumour necrosis factor on lipid metabolism (Table 6) suggest that they may act in concert *in vivo*. This view is strengthened by the finding that tumour necrosis factor can stimulate interleukin-1 secretion *in vivo* and *in vitro* (Bachwich *et al.*, 1986; Dinarello *et al.*, 1986). The reverse is also true (Nawroth *et al.*, 1986). In contrast with the two cytokines, tumour growth itself did not alter lipid absorption or lipid accumulation in the lactating mammary gland (Evans & Williamson, 1988a); the effects on lipid metabolism appeared to be restricted to adipose tissue (Table 6). This explains the absence of hypertriglyceridaemia in tumour-bearing lactating rats (Evans & Williamson, 1988a), because lipid

Table 6. Comparison of the effects of interleukin-1, tumour necrosis factor or tumour growth on exogenous [^{14}C]lipid metabolism in the rat

The information in this Table was compiled from the results in the present paper and in those of Evans & Williamson (1988a,b). The changes are relative to control (virgin, lactating or litter-removed) rats.

Measurement	Effector ... Interleukin-1	Tumour necrosis factor- α	Tumour growth
Lipid absorption	Decreased	Decreased	Unchanged
Lipid oxidation	Decreased	Decreased	Decreased
Lipid accumulation			
White adipose tissue	Decreased*	Decreased*	Decreased
Brown adipose tissue	Decreased*	Decreased*	Unchanged
Lactating mammary gland	Decreased	Decreased	Unchanged
Lipoprotein lipase activity			
White adipose tissue	Unchanged	Decreased	Decreased
Heart	Unchanged†	Unchanged	—
Lactating mammary gland	Unchanged	Decreased	Unchanged
Plasma triacylglycerols	Increased	Increased	Increased*

* Not in lactating rats.

† Decreased in lactation.

deposition is depressed in adipose tissue and enhanced in mammary gland during lactation (Oller do Nascimento & Williamson, 1986). Thus tumour growth, at least in the case of the Walker 256 carcinoma, appears to be more tissue-specific in its actions on lipid metabolism, which suggests that factors other than tumour necrosis factor or interleukin-1 may be involved in its effects.

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