EFFECT OF THE HYPOPHYSEAL PREPARATION ADIPOSIN ON THE LIPOLYTIC ACTIVITY OF ADIPOSE TISSUE AND ON THE SERUM CONCENTRATION OF FREE HIGHER FATTY ACIDS

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In 1956, a preparation was obtained from the hypophyses of cattle and pigs [2] which, if injected subcutaneously into mice, caused a transient increase in the content of lipids in the liver without any reduction in the glycogen content, and if injected into rabbits, rats and mice, caused a transient increase in the oxidation products of fatty acids (ketone bodies), while if repeated injections were given the gain in weight of the animals was retarded. In the doses used, the preparation was found to contain no somatotropic, adrenocorticotropic, thyrotropic, gonadotropic, or lactogenic hormones. Its active principle was called "adiposin," and it was concluded that it had a specific lipid-mobilizing (adipokinetic) action. Further researches [1, 3] showed that adiposin lowers the respiratory quotient in mice of normal weight and with experimental obesity, and thus that it stimulates the oxidation of lipids.

After the discovery [4-9] that lipids are released from adipose tissue not so much as triglycerides (neutral lipids) as in the form of nonesterified (free) higher fatty acids (NEFA), the principal criterion of mobilization of lipids has become an increase in their concentration in the blood, and, in experimental conditions in vitro, stimulation of lipolysis in adipose tissue with release of NEFA into the incubation medium.

We have investigated the effect of adiposin on the lipolytic activity of adipose tissue in vitro and in vivo. At the same time the concentration of NEFA in the serum was studied. Since an increase in the glucose concentration inhibits lipolysis of adipose tissue [4, 6, 8, 9], we also studied by means of experiments in vitro the effect of addition of glucose to the incubation medium on the lipolytic action of adiposin. Experiments were also performed to compare the effect of adiposin and the somatotropic hormone of the hypophysis (SH) on the lipolysis of adipose tissue. SH also possesses lipid-mobilizing activity [3, 4, 8, 9].

EXPERIMENTAL METHOD

The experimental animals were albino rats (male) weighing 130-200 g. We used adiposin (batch No. $82a_2$) and SH from the experimental production laboratory of the All-Union Institute of Experimental Endocrinology. The lipolytic activity of the epididymal adipose tissue was determined by the method of Gordon and Cherkes [5], i.e., by the difference between the concentration of NEFA in the incubation medium before and after incubation (150 min in Krebs-Ringer phosphate buffer, pH 7.3-7.4, with 5% albumin), and expressed as microequivalents in 1 ml NEFA per 1 g adipose tissue. The NEFA were determined by Dole's method [7].

EXPERIMENTAL RESULTS

The addition of adiposin in a dose of 0.1 and 0.01 mg/ml to the medium considerably increased the lipolytic activity of the adipose tissue (Table 1).

Addition of the preparation in a dose of 0.1 mg/ml caused an average increase of 114% in the release of NEFA, while a dose of 0.01 mg/ml caused an increase of 50%. It must be pointed out that SH, in the same dose (0.01 mg/ml) increased lipolysis by only 35% on the average. The addition of glucose to the incubation medium inhibited the lipolytic activity of the adipose tissue, corresponding to its utilization of glucose (Table 2).

A glucose concentration of 50 mg% in the incubation fluid depressed lipolysis on the average by 67%, and a concentration of 300 mg% caused a depression of 94%. The addition of glucose in the same concentrations to medium

TABLE 1. Effect of Adiposin on the Lipolytic Activity of Adipose Tissue and the Effect of Addition of Glucose on These Processes (mean data)

Agent	Lipolytic activity		Lipolytic activity on addition of 0.025 ml of 2% glucose to 1 ml of medium (50 mg%)	Lipolytic activity on addition of 0.03 ml of 10% glucose to 1 ml of medium (300 mg%)
	control (no addition of adiposin or SH)	experiment		
Adiposin (0.1 mg in 1 ml of medium)	5.27 ± 0.5 (14)	11.3 ± 0.89 (14) P < 0.001 +114%	6.4 ± 0.89 (14) P < 0.001 − 43%	6.2 ± 0.88 (14) P < 0.001 − 45%
Adiposin (0.01 mg in 1 ml of medium)	3.4 ± 0.19 (14)	5.1 ± 0.32 (14) P < 0.001 + 50%	3.3 ± 0.29 (14) P < 0.001 − 35%	3.2 ± 0.29 (14) P < 0.001 − 37%
SH (0.01 mg in 1 ml of medium)	2.5 ± 0.24 (10)	3.38 ± 0.26 (10) P < 0.05 + 35%	2.24 ± 0.28 (10) P < 0.01 − 33%	2.24 ± 0.28 (10) P < 0.01 − 33%

Notes. 1. The lipolytic activity is the difference between the NEFA concentration before and after incubation (150 min), expressed in microequivalents in 1 ml/1 g tissue. 2. The number of experiments is given in parentheses.

TABLE 2. Lipolytic Activity and Glucose Absorption by Epididymal Adipose Tissue of Rats Without and With Addition of Glucose (mean data)

Lipolytic activity	Lipolytic activity with a glucose concentration of		Glucose absorption (in mg%) at a concentration of	
	50 mg%	300 mg%	50 mg%	300 mg%
4,85±0,595 (11)	1,58±0,522 (11) P<0,001 (—67,4%)	0,261±0,371 (11) P<0,001 (—94,6%)	10,3±2,01 (10)	24,0±7,72 (10)

with adiposin also depressed the activation of lipolysis in the adipose tissue by this preparation, but to a much lesser degree than in the experiments without addition of adiposin. The same was observed after addition of glucose to the medium with SH. In the experiments with both adiposin and SH, the adipose tissue utilized glucose to the same extent as in control investigations without the addition of these preparations. Hence, the action of glucose in inhibiting lipolysis was weakened in the presence of adiposin.

Depression of the release of NEFA from adipose tissue by glucose is due to the fact that it stimulates synthesis of triglycerides [6, 8, 9]. Hence, it may be assumed that adiposin not only stimulates lipolysis, but also inhibits the synthesis of triglycerides in adipose tissue.

When rats were given a subcutaneous injection of adiposin in a dose of 1.5 mg/100 g, and the epididymal adipose tissue was extracted 30 and 60 min thereafter, activation of its lipolysis was also observed, and it was especially marked 60 min after injection (Table 3). The NEFA concentration in the serum was considerably increased at the same time.

Hence, in experiments both in vivo and in vitro adiposin considerably increased the lipolytic activity of adipose tissue, i.e., stimulated the mobilization of its higher nonesterified (free) fatty acids, resulting in an increase in their concentration in the serum. This effect in experiments in vitro was more marked than after addition of the same dose

TABLE 3. Effect of Subcutaneous Injection of Adiposin (1.5 mg/100 g) on the Lipolytic Activity of Epididymal Adipose Tissue and on the Serum NEFA Concentration in Rats (mean data)

Agent	Time of investigation after injection of adiposin (min)	No. of animals	Lipolytic activity of adipose tissue	No. of animals	Serum NEFA concentration (in μEq/liter)
Control	—	10	2,5±0,24	22	1,08±0,046
Adiposin	30	5	5,2±0,5 $P<0,001$ +108%	5	1,76±0,13 $P<0,001$ +63%
Adiposin	60	10	8,0±0,31 $P<0,001$ +220%	10	2,17±0,023 $P<0,001$ +100%

of SH. The suppression of the inhibitory action of glucose on lipolysis of adipose tissue by adiposin suggests that the latter not only stimulates the lipolytic activity of adipose tissue, but also inhibits synthesis of triglycerides in adipose tissue.

It may be concluded from our results that the lipid-mobilizing (adipokinetic) effect of adiposin is due both to activation of lipolysis in adipose tissue and to inhibition of synthesis of triglycerides in that tissue.

SUMMARY

Subject to study was the effect produced by adiposin, a hypophyseal preparation obtained by S. M. Leites and A. A. Molchanova, on the lipolytic activity of adipose tissue and the NEFA content in the rat serum. In experiments in vitro and in vivo a demonstration was made of the activating effect produced by low doses of adiposin (0.01 mg in vitro and 1.5 mg – in vivo) on NEFA exit from the adipose tissue with a parallel considerable rise in their content in the serum. Adiposin also retards glucose inhibition of lipolysis in the adipose tissue. It is supposed that adipokinetic affect of adiposin is due not only to activation of lipolysis by it in the adipose tissue, but also to the triglyceride synthesis in the latter.

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