significant ($p < 0.01$, $p < 0.001$ respectively). However, allicin is only 64% as active in hypoglycemic action and 47% as active in reducing the G:N ratio, compared with the effects of tolbutamide. Rediction in the G:N ratio is a measure of the improvement in the capacity of the diabetic animal to utilize the glucose derived from protein.

Discussion. The improvement in the diabetic condition of the animals brought about by tolbutamide and allicin may be dependent on the insulin reserves of the animals, reported previously[1]. The inability of these drugs to produce a greater fall in the blood sugar of diabetic animals may be due to several unknown factors which control the hyperglycemic condition of alloxan diabetes. The action of oral hypoglycemic drugs is much dependent on endogenous and exogenous sources of insulin[9]. The control of hyperglycemia in alloxan diabetes is possible by oral drugs provided the blood sugar levels are near normal[10]. Ketosis and hyperlipaemia may be other factors which prevent the lowering of blood sugar beyond a particular range. However the hypoglycemic action of allicin at dosages of 0.05 g to 0.25 g/kg is significant ($p < 0.05$–0.005), whilst that of tolbutamide at a standard dose of 0.25 g/kg is even more marked ($p < 0.001$). An improvement is definitely observed in the diabetic condition of the animals as evident from the reduction in G:N ratio on a short-term treatment with the drugs. Studies employing higher dosages on long-term treatment of diabetic animals are warranted. In a previous study[11] the effects of allicin at a dosage of 100 mg/kg/day on long-term feeding to normal rats were examined. There was a significant reduction in lipid constituents of blood and liver on allicin treatment. In this respect allicin might have an advantage over tolbutamide which has been shown to produce hyperlipaemia under certain conditions[12,13]. Very recently also reports supporting the beneficial uses of garlic and onion in the treatment of diabetes were made by some physicians[14]. All these findings justify further studies on the therapeutic effects of these vegetables which are rich in allicin type compounds[15–17]. The blood fibrinolytic effect of garlic has been attributed to its oil[18], and a preliminary study[19], conducted by the author at the Royal Victoria Infirmary of Newcastle-upon-Tyne, revealed that allicin is one of the sulphur compounds with blood fibrinolytic action.

Summary. On oral administration to alloxan diabetic rabbits, allicin produces an increase in its hypoglycemic action with relation to dose. A short-term treatment with allicin, as well as with tolbutamide, significantly reduced the blood sugar levels and glucose nitrogen ratio of the above animals.

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Effects of Tryptophan and Other Amino Acids on Glucose Uptake and Carbon Dioxide Output by the Insulin-Stimulated Adipose Tissue

The i.v. infusion of amino acid mixtures to healthy subjects produces an initial increase in blood glucose followed by a decrease below control levels[1,2]. These effects are explained by the stimulating action of amino acids on glucagon[3,4] and insulin[1,2] secretion. However, the possible contribution to the glycemia changes of a direct action of amino acids on glucose utilization by peripheral tissues has scarcely been investigated. Such a direct action has been suggested as a way in which some amino acids might prevent epinephrine hyperglycemia, both in normal and in alloxan diabetic rats[5]. The present paper deals with the effects of 7 amino acids on glucose utilization by the rat adipose tissue in vitro.

Materials and methods. Male Wistar rats (90–120 g), fed ad libitum, were killed by decapitation. 2 portions of epididymal fat pad (about 200 mg), one from each side, were removed, weighed and placed into 2 Warburg vessels containing 2 ml of incubation medium. From each animal, one portion was incubated in medium without amino acids (control) and the other one in the same medium containing the appropriate amino acid (experimental). Total gas exchange of the tissue was determined as described by Ball et al.[6]; the incubation medium in this case was Krebs-Ringer-bicarbonate saline[7], pH 7.4, with 10 m*M* glucose, and 5% CO_2–95% O_2 as gas phase. When O_2 uptake was determined, the saline solution was Krebs-Ringer-phosphate[7], pH 7.4, with 100% O_2 as gas phase. Insulin (Nordisk Insulinlaboratorium, Copenhagen) was added to the medium either before putting into it the tissue or after a period of incubation at 37 °C, to give a final concentration of 10^3–10^5 μU/ml. Manometric readings were carried out during 60–120 min at 37 °C. Glucose and lactate were determined by a glucose-oxidase and a lactate-dehydrogenase method, using analytical kits from Boehringer, Mannheim. Amino acids (L-isomers) were purchased from Sigma, London. The Student paired *t*-test was applied for comparations between control and experimental values.

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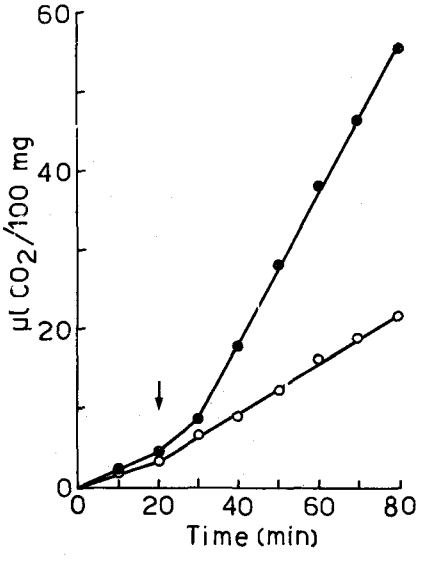
Effects of several amino acids on CO_2 output and on glucose uptake by adipose tissue

Amino acid	Concentration (m*M*)	No. of animals	CO_2 output µl/100 mg/h		Glucose uptake µmoles/100 mg/h)	
			Control	Experimental	Control	Experimental
Leucine	10	4	58.3 ± 5.8	59.8 ± 3.9	1.69 ± 0.08	1.64 ± 0.09
Proline	10	4	63.2 ± 10.8	60.8 ± 10.6	1.62 ± 0.11	1.60 ± 0.14
Histidine	10	6	48.8 ± 5.9	43.4 ± 5.9[b]	1.41 ± 0.19	1.17 ± 0.13
Arginine	10	6	65.6 ± 6.8	56.4 ± 5.4[b]	1.84 ± 0.15	1.72 ± 0.14
Alanine	10	10	59.0 ± 3.4	48.9 ± 4.1[b]	1.81 ± 0.18	1.54 ± 0.15[a]
Phenylalanine	10	6	62.0 ± 7.0	47.8 ± 4.2[b]	1.78 ± 0.09	1.53 ± 0.07[a]
Tryptophan	0.5	4	52.9 ± 5.7	48.0 ± 4.0	1.61 ± 0.17	1.55 ± 0.13
Tryptophan	1	4	51.9 ± 6.7	49.7 ± 6.8	1.50 ± 0.11	1.51 ± 0.12
Tryptophan	4	4	57.9 ± 3.4	44.3 ± 2.6[a]	1.65 ± 0.10	1.30 ± 0.10[a]
Tryptophan	10	14	50.4 ± 4.7	18.4 ± 1.9[c]	1.51 ± 0.12	0.87 ± 0.08[c]
Tryptophan	10	8	8.5 ± 1.4	4.0 ± 0.9[a]	0.37 ± 0.08	0.40 ± 0.04

The incubation medium contained exogenous insulin at a concentration of 10^5 µU/ml, except in those experiments with tryptophan in the last row in which no exogenous insulin was added. Values are means ± SE. [a] $P < 0.05$; [b] $p < 0.01$; [c] $p < 0.001$.

Results. The time course of CO_2 output by adipose tissue in a typical experiment is shown in the Figure. The Table summarizes the effects of 7 amino acids on CO_2 output and glucose uptake. With exogenous insulin in the medium, CO_2 output was significantly reduced in presence of 10 m*M* of either histidine, arginine, alanine, phenylalanine or tryptophan, the inhibition by tryptophan (64%) being notably greater than that exerted by the other amino acids (10–20%). In each case there was a parallel diminution of glucose uptake by the tissue. A significant inhibition of both CO_2 output and glucose uptake was also found with 4 m*M* tryptophan, but lower concentrations of this amino acid did not produce inhibition. In absence of exogenous insulin, 10 m*M* tryptophan also inhibited the CO_2 output by the tissue, without a significant effect on glucose uptake.

Oxygen uptake by adipose tissue incubated with exogenous insulin was not modified by the presence of amino acids in the medium. In experiments with 10 m*M* tryptophan, which produced the maximal inhibition on both CO_2 output and glucose uptake, the values of O_2 uptake were (mean ± SE, $n = 6$) 23.8 ± 2.4 µl/100 mg/h for controls, and 21.7 ± 1.6 µl/100 mg/h in presence of the amino acid. Lactate production by the tissue was determined in the 14 experiments with 10 m*M* tryptophan and exogenous insulin referred to in the Table. The mean values (±SE) were 0.26 ± 0.04 µmoles/100 mg/h for controls, and 0.10 ± 0.01 µmoles/100 mg/h in presence of amino acid ($p < 0.001$). From these data it can be calculated that only about 10% of the difference in CO_2 output between control and experimental vessels could be accounted for by the difference in lactate production and buffering in the bicarbonate medium.



Time course of CO_2 output by adipose tissue in a typical experiment. 2 portions of epididymal fat pad from the same animal were incubated either without added amino acids (●) or with 10 m*M* tryptophan (○). At the time indicated by the arrow, 0.1 ml of insulin solution was added from the side arms of the 2 vessels, to yield a concentration in the medium of 10^3 µU/ml.

Discussion. Our results suggest that some amino acids decrease the insulin-stimulated glucose metabolism in adipose tissue. However, these inhibitory effects are so small, except in the case of tryptophan, and require such a high concentration of amino acids, that it is improbable that they should result in a significant change of glycemia in vivo.

In the case of tryptophan, our results agree with previous observations. This amino acid inhibits the insulin stimulation of proline and 3-*O*-methylglucose transport in the isolated rat diaphragm[8], and it also inhibits the insulin stimulation of protein synthesis in the same preparation[9]. Tryptophan forms a complex with insulin in solution[10], and in this way it might hinder the hormon-receptor interactions. However, this explanation can not be applied to the inhibitory mechanism of insulin effects in adipose tissue exerted by the other amino acids.

Summary. Tryptophan (4–10 m*M*) reduces the stimulating effect of insulin on glucose uptake, CO_2 output and lactate production by adipose tissue. Similar but lesser effects were also obtained with high concentrations of other amino acids.

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