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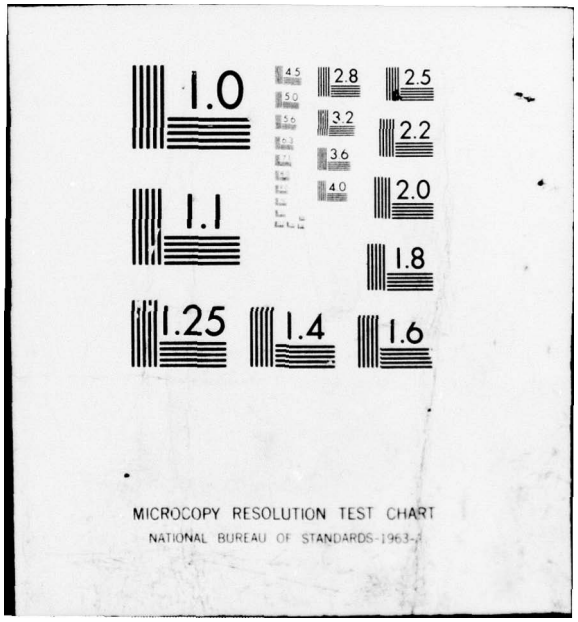
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MUL 0536

Dokshina, G.A., Silaeva, T. Yu., Yartsev, Ye.I.

INSULIN-LIKE EFFECTS OF TAURINE

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Vopr Med Khim 22:503-6, 1976

ABSTRACT: A one-time injection of taurine in a dose of 200 mg/kg will increase insulin-like activity in rat plasma, doubles the glycogen content of the liver and decreases glycemia. In in vitro experiments taurine increases glucose absorption by isolated diaphragms and raises insulin activity. On the basis of increased adenylacyclase activity in incubated diaphragms upon introduction of taurine and insulin-like action of 3',5'-AMF and theophylline, the conclusion was made that the insulin-like effect of taurine is mediated through cyclic AMF.

Deep disruptions of hydrocarbon exchange that develop during various forms of diabetes, cirrhosis of the liver, radiation sickness and other diseases are caused, evidently, by a functional inadequacy of the insulin apparatus of the pancreas. Therefore, at present research is being conducted experimentally to find preparations that possess insulinogenic activity or the capacity to make potent the action of insulin.

Research by a number of authors /1/ demonstrated the potency-causing effect of taurine on the hypoglycemic effect of insulin. However, one of these authors gives a

negative answer to the question of an independent insulin-like effect of taurine on glycemia in rats and glucose absorption by diaphragmal tissue. At the same time, earlier studies /2/ indicated the capacity of taurine to cause the hypoglycemic effect in dogs. Taking into account the utilization of taurine in clinical practice /3-5/ and its wide metabolic spectrum of action, established in experimental research /6/, it became reasonable to study the effect of taurine on hydrocarbon exchange in intact animals.

Material and Methods

The research was carried out on white rats of both sexes weighing between 150 and 200 g. In in vivo experiments the 1st group of rats received intraperitonially insulin calculated at 0.2 units/kg. The 2nd received taurine (200 mg/kg). The 3d received both preparations together. A one-time introduction of the preparations was used, with subsequent decapitation of the animals after 6 hours, 1, 2, 3 hours, and administration for a period of 7 days daily, with decapitation on the 8th day. The insulin-like activity of the blood plasma (ILA) was determined according to the absorption of glucose by diaphragmal tissue, after preliminary isolation of KU-2 on ion-exchange resins using the described method /7/, blood sugar -- according to Kats et al. /8/, liver glyco-

gen -- according to Hood and Somogi /9/.

In the in vitro experiments diaphragms from hungry rats weighing 100 g were extracted rapidly, divided into 2 parts and placed into Erlenmeyer flasks, 20 ml in volume, containing a saturated gaseous mixture (CO_2: O_2 -- 5%:95%) Krebs-Henselait buffer, glucose in a concentration of 400 mg%, taurine -- 10^{-6}, $2x10^{-5}$, 10^{-3}, 10^{-2}M: theophylline -- $6x10^{-3}$M; 3',5'-AMF -- 10^{-3}M: insulin -- 0.1 and 1 unit/ml. After introduction of these substances the flasks were again saturated with gaseous mixture and incubated in a water bath at 37° and 120 rockings/min for 3 hours.

Adenylatcyclase activity was expressed in micromoles of cyclic 3',5'-AMF, formed from ATF on 100 mg of diaphragm. The ground tissue was incubated at 37° for 3 hours. 3',5'-AMF was identified chromatographically on paper in the system propanol-ammonia-water (7:1:2).

Results and Discussion

During one-time injection of taurine in a dose of 200 mg/kg (Table 1) the plasma ILA increased, the glycogen content in the liver doubled and the glucose concentration in the blood decreased.

These effects were found 6 hours following taurine administration (Table 2). However, the increase in plasma ILA and hypoglycemia disappeared by the 2nd day after admi-

nistration. The glycogen content in the liver was restored after 72 hours.

The administration of insulin in this series of experiments (as a comparison with taurine) caused an increase in the liver glycogen content for 2 to 3 days, without a change in the ILA and sugar level in the blood. The course of administration of preparations during 7 days in the identical dosages (Table 3) increased plasma ILA to 3.4± 0.4 mg, and liver glycogen to 41.3±3.7 mg/g only with simultaneous use of taurine and insulin. The hypoglycemic effect was observed in all 3 experimental series. It should be stressed that with simultaneous introduction of taurine and insulin there was manifested a combined affect of the preparations.

TABLE 1. Changes in plasma ILA, liver glycogen and blood sugar content in intact rats during one-time administration of taurine

Experimental conditions	ILA (in mg glucose per 100 g tissue in 3 hours)	Glycogen (in mg per 1 g tissue)	Sugar (mg %)
Control	2,75± 0,3 (6) 2,74± 0,7 (8)	27,0± 6,3 (8) 37,0± 1,4 (4) $P>0,05$	103,0± 0,6 (5) 102,0± 0,07 (4)
Taurine (100 mg/kg)			
Taurine (200 mg/kg)	3,30±0,005 (9) $P=0,05$	54,5±1,3 (12) $P<0,01$	90,0± 0,07 (10) $P<0,01$

NOTE: Here and in Table 2 the number of experiments is in parentheses.

TABLE 2. Changes in blood ILA, liver glycogen and blood sugar content in rats after administration of taurine (200 mg/kg) and insulin (0.2 units/kg).

(1) Сроки после введения препарата	ИЛА (поглощение глюкозы в мг на 100 г диафрагмы за 3 ч) (2)		Гликоген (в мг на 1 г ткани) (3)
	таурин (4)	инсулин (5)	таурин (4)
Контроль Control after	2,75± 0,3 (6)	2,75± 0,3 (6)	27,0± 6,3 (8)
Через 6 ч 6 hours	3,11± 0,18 (7)	2,74± 0,7 (7)	50,2± 6,3 (9)
	$P>0,3$	$P>0,9$	$P<0,05$
1-е сутки DAY 1	3,30± 0,005 (9)	—	54,5± 1,3 (12)
	$P=0,05$		$P<0,01$
2-е сутки DAY 2	3,00± 1,8 (7)	2,74± 0,6 (6)	41,4± 3,8 (10)
	$P>0,9$	$P>0,9$	$P=0,05$
3-и сутки DAY 3	3,04± 1,2 (4)	2,79± 0,9 (6)	36,4± 3,2
	$P>0,8$	$P>0,9$	$P>0,5$

(1) Сроки после введения препарата	Гликоген (в мг на 1 г ткани) (3)	(6) Сахар (в мг%)	
	(5) инсулин	(4) таурин	(5) инсулин
Контроль CONTROL AFTER	27,0± 0,3 (8)	103,0± 0,6 (5)	103,0± 0,6 (5)
Через 6 ч 6 HOURS	36,7± 1,4 (4)	90,0± 0,08 (6)	102,0± 0,05 (6)
	$P<0,05$	$P<0,02$	$P>0,05$
1-е сутки DAY 1	—	90,0± 0,7 (10)	—
		$P<0,02$	
2-е сутки DAY 2	40,3± 0,6 (4)	101,0± 0,03 (7)	101,0± 0,1 (6)
	$P=0,05$	$P>0,05$	$P>0,05$
3-и сутки DAY 3	31,0± 6,1	—	101,4± 0,01
	$P>0,05$		$P>0,05$

Key to table 2: 1) Period of time after administration of the preparation; 2) ILA (glucose absorption in mg per 100 g diaphragm in 3 hours); 3) Glycogen (in mg per 1 g tissue; 4) Taurine; 5) Insulin; 6) Sugar (in mg %).

The data obtained provided evidence of the independent insulin-like and potency-causing action of taurine. The possibility of these effects was studied in the next series of experiments on isolated rat diaphragms.

The experimental data are presented in Figure 1. They demonstrate that the introduction of taurine into an

incubation medium containing insulin increases the absorption of glucose (see fig. 1, 1) in strict dependence on the taurine concentration. Maximum glucose absorption in the presence of insulin and taurine comprised 3.77±0.01 mg as against 1.5±0.01 mg in the control (insulin alone -- 0.1 units/ml). When instead of the insulin solution eluate of plasma was taken, then the glucose absorption speed was greater (see fig. 1, 2). Upon the introduction of taurine into an incubation medium,lacking insulin, in a concentration of 10^{-3}, 10^{-2}M (see Fig. 1, 3) the rat diaphragms absorbed 2 times as much glucose (2.2±0.01: 2.45±0.3 mg, respectively) than in the control (1.04±0.03 mg). However, it should be noted that the simultaneous presence of insulin in the medium (0.1 units/ml) or of eluate of plasma and taurine, caused more intensive absorption.

TABLE 3. Changes in ILA of blood, liver glycogen and blood sugar content in rats after a course of taurine administration (200 mg/kg) and taurine with insulin (0.2 units/kg)

Experimental conditions	ILA (glucose absorption in mg per 100 g diaphragm over 3 hrs)	Glycogen (mg per 1 g tissue)	Sugar (mg%)
Control	2,75± 0,3 (6)	27,0± 6,3 (6)	103,0± 0,06 (6)
Taurine	3,13± 0,001 (6) $P>0,7$	36,3± 0,01 (7) $P>0,8$	95,0± 0,003 (7) $P<0,01$
Insulin	3,19± 1,6 (4) $P>0,8$	32,0± 3,1 (4) $P-0,4$	91,0± 0,3 (4) $P<0,01$
Taurine + insulin	3,4± 0,4 (4) $P-0,05$	41,3± 3,7 (4) $P<0,05$	86,0± 0,03 (7) $P<0,05$

Thus, the in vitro experimental results showed that, on the one hand, the introduction of taurine into the incubation medium causes a further increase in glucose consumption by isolated diaphragms in the presence of insulin, and on the other -- taurine gives a kind of independent insulin-like effect with respect to glucose absorption by tissues.

The results obtained, like the research by Edelman et al. /10/, who observed increased glucose absorption from the incubation medium upon addition of 3',5'-AMF, brought us to the thought concerning the participation of cyclic AMF in the creation of the independent insulin-like effect of taurine. It turned out that cyclic AMF (10^{-3}M) and theophylline (6 mM) also increased glucose absorption, but to a lesser degree than did taurine (Fig. 2). Insulin (1 unit/ml), as a known stimulant of glucose absorption by diaphragm tissue, caused a greater absorption effect (3.10±0.09 mg) than taurine, 3',5'-AMF and theophylline.

Thus, the administration of taurine to intact animals, evidently, creates favorable antecedents for the synthesis of liver glycogen at the expense of utilization of the glucose by tissue. This effect of taurine may become realized at the expense of increased hormone secretion and, as the in vitro experiments demonstrate, at the expense of its direct participation in the active

transport of glucose. The slight hypoglycemia that develops with the introduction of taurine is partial proof of our suppositions and supports the data indicating that taurine is favorable to the utilization of sugar by the organism /2,5/.

The stimulation by taurine of glucose absorption by diaphragm tissue is possibly realized through the system cyclo-AMF, since the addition into the incubation medium of 3',5'-AMF and theophylline -- a specific inhibitor of phosphodiesterase -- strengthens this process even more. The supposition that taurine acts upon the adenylatcyclase activity of tissue was supported in the experiments with the direct determination of adenylatcyclase activity in the incubating diaphragms. It was demonstrated that taurine, with a high degree of reliability (P less than 0.001) increases ferment activity (from 0.266 ± 0.001 to 0.311 ± 0.006 mkmole 3',5'-AMF).

A similar direction for the regulation with taurine of glucose utilization by tissue and glycogen biosynthesis may take place in the organism, which does not exclude, however, its simultaneous potency-causing effect on the activity of insulin.

The authors express their thanks to V.G. Yakovlev for the taurine preparation, and to G.A. Sukhanova for her assistance in the work.

FIGURE 1. The effect of insulin (1), eluate of plasma of intact animals (2) and taurine (3) on glucose absorption by isolated rat diaphragms.

Along the abscissa: taurine concentration (M): along the ordinate axis: glucose absorption speed (in mg per 100 g of diaphragm tissue over 3 hours)

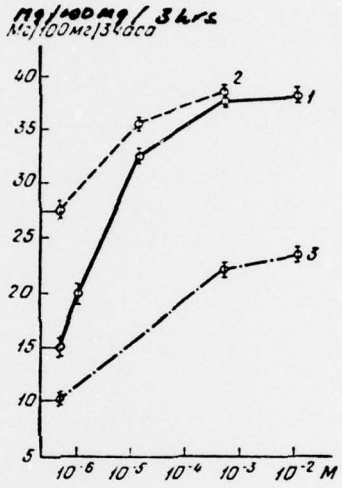
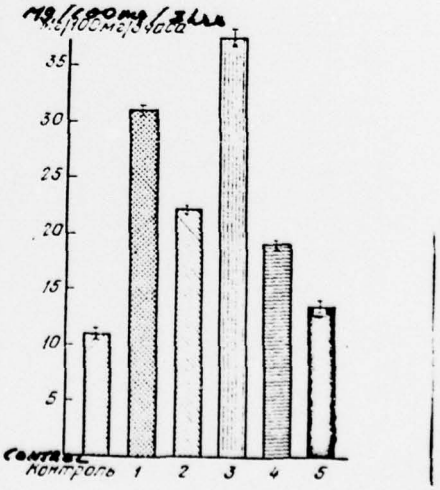


FIGURE 2. The effect of 1 unit/ml insulin (1): 10^{-3}M taurine (2): 10^{-3}M taurine per +0.1 unit/ml insulin (3): 10^{-3}M 3',5'-AMF (4): 6 mM theophylline (5) on glucose absorption by diaphragm tissue.



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