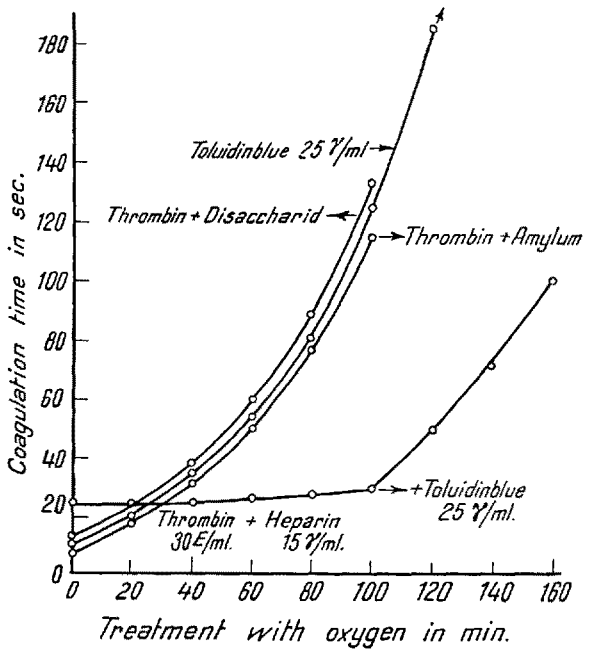
The present work demonstrates a property of heparin, unknown till now, from which one could conclude–under certain circumstances–on a thrombin-protecting effect of the heparin.

In a previous work[1] it was reported, that thrombin is oxidizable and that it loses its coagulation activity in this oxidized form. In the actual work the oxidation of thrombin could be reached by streaming it through with molecular oxygen, as our starting material (thrombin, Hoffmann - La Roche) contains some unknown compound which activates molecular oxygen. This proceeding can be shown in a typical curve (see Figure). It is evident from this curve that thrombin loses its activity to coagulate plasma (0·2% sodium oxalate) or fibrinogen (0·6%) gradually and finally gets inactive totally, when it is streamed through with oxygen.

If heparin up to a concentration of 15 γ/ml is added to a solution of thrombin the coagulation time against plasma increases from 10 to 26 seconds. When, on the other hand, the same heparin thrombin mixture and the solution of thrombin whithout heparin are streamed through with oxygen at the same time, so the heparin-free solution of thrombin only loses its coagulation activity, meanwhile the mixture of thrombin and heparin keeps its original coagulation activity completely.

Therefore heparin protects the thrombin from oxidation by oxygen.



As the heparin is an esterified polysaccharide (Liquemin, Hoffmann-La Roche ester of polysulfuric acid of mucoitin), the experiment was repeated with other non-esterified saccharides. It was shown that neither disaccharides nor the polysaccharide starch has the oxidation-inhibiting quality of heparin.

The specific activity of heparin is proved by the fact that, if the heparin in the mixture of thrombin and heparin is combined with toluidine blue (25 γ/ml) the activity of heparin is excluded and an oxidation resp. inactivation of thrombin takes place (see Figure).

[1] L. A. PÁLOS, Nature, in print.

Experiments on the behaviour of heparin during oxidation of the plasma and the other coagulation factors, are in process.

The acting mechanism of heparin in this reaction is not known and should be further investigated.

L. A. PÁLOS

Institute for Hygiene and Bacteriology of the University of Basle, Switzerland, December 30, 1948.

Zusammenfassung

Das Thrombin ist oxydierbar und wird in seiner oxydierten Form inaktiv. Die Oxydation des Thrombins kann durch sehr kleine Mengen Heparin gehemmt werden. Wenn das Heparin mit Toluidinblau gebunden wird, kann die Oxydation vor sich gehen.

Effect of Thiamin, Riboflavin, Pyridoxin, and Nicotinic Acid on the Intestinal Absorption of Dextrose

In earlier experiments[1] I found that after the administration of unphysiologically large doses of a vitamin used in the metabolism in phosphorylated form, the apparatus of the phosphorylation becomes exhausted. I further found[2] that the absorption of one vitamin—in my experiments that of thiamin—from the intestine was greatly impaired, when other vitamins of the B complex were given in large doses before the experiment. This fact could also be demonstrated by using dextrose instead of the vitamins. So I could explain the cases of the so-called vitamin imbalance, i. e. the deficiency symptoms which became manifest in a deficiency state during the treatment with large doses of a single vitamin, symptoms of pellagra, for instance, after administration of riboflavin, or symptoms of polyneuritis during the treatment with nicotinic acid. The high unphysiological dosis of a vitamin gives rise to the exhaustion of the phosphorylation apparatus and other vitamins cannot be utilized.

To get further evidences of my hypothesis, I examined the absorption of dextrose–a substance which must be phosphorylated too when absorbed and utilized–from the intestine of rats, after having administered large doses of the B-complex vitamins.

My method was that of LASZT's procedure[3] in which 200 mg of dextrose in 2 cc phys. sodium chloride solution were given into a 30 cm long tied bowel section of narcotized rats and after 30 minutes the unabsorbed quantity of the dextrose was determined. Details of the method are given elsewhere[2].

The results of the control experiments were the following:

Table I

No.	mg dextrose found after 30 min.	mg dextrose absorbed	absorbed dextrose %
1	120	80	40
2	137	63	31
3	112	88	44
4	121	79	38
5	109	91	45
6	124	76	38

[1] I. MAGYAR, Acta medica Hungarica *1*, 46 (1948).
[2] I. MAGYAR, Int. Z. Vitaminforsch., in print.
[3] L. LASZT and L. DALLA TORRE, Schweiz. med. Wschr. *22*, 1416 (1941).

In further experiments, 60 minutes before the administration of dextrose into the bowel the animals were given subcutaneously 50 mg of thiamin, 5 mg of riboflavin, 25 mg of pyridoxin and 100 mg of nicotinamide respectively.

Table II

No.	Vitamin given before	mg dextrose found after 30 min.	mg dextrose absorbed	absorbed dextrose %
1	thiamin	178	22	11
2	,,	187	13	6
3	,,	180	20	10
4	,,	189	11	5
5	,,	174	26	13
6	riboflavin	196	4	2
7	,,	189	11	5
8	,,	200	—	—
9	nicotinamide	187	13	6
10	,,	200	—	—
11	,,	192	8	4
12	pyridoxin	174	26	13
13	,,	178	22	11
14	,,	196	4	2

It can be seen from the tables that *vitamins of the B complex (thiamin, riboflavin, nicotinic acid and pyridoxin) decrease the absorption rate of sugar from the bowel.*

According to my view, this effect depends on the exhaustion of the phosphorylation—may be on the exhaustion of the enzyme phosphorylase—if large doses of the vitamins are given, whereby dextrose, needing also phosphorylation, becomes incompletely absorbed and used.

IMRE MAGYAR

First Medical Clinic of the University of Budapest, July 30, 1948.

Zusammenfassung

Die Vitamine des B-Komplexes vermindern die Zuckerresorption im Darm. Durch die Phosphorylierung von Thiamin, Riboflavin, Nikotinsäure und Pyridoxin wird – wahrscheinlich – die Phosphorylase erschöpft. Dextrose, die phosphoryliert werden muß, kann dann nur in kleinerer Menge resorbiert und verbraucht werden.

Inhibitory Effect of Simultaneous Administration of Antasten and Tween 20 on Gastric Secretion Induced by Histamine or Vagal Stimulation

IVY *et. al.*[1] have recently shown that the wetting agent Tween 20 which is a polyoxylene derivate of sorbitan monolaurate, produces urticaria when given intravenously in dogs. GROSSMAN and ROBERTSON[2] then found that the urticaria is accompanied by gastric secretion which they were able to prevent or reduce by pre-treatment with Benadryl (β-dimethylaminoethyl benzhydryl ether hydrochloride) Inasmuch as Benadryl does not inhibit histamine-stimulated gastric secretion, they thought that the mode of action of Benadryl on secretion stimulated by Tween 20 must involve another mechanism. They stated that if histamine is released when Tween 20 is administered, Benadryl must block its formation and not its action on the gastric glands.

[1] A. C. IVY, C. A. TANTURI, R. HERNANDEZ, and E. BAROSO, Arch. Derm., in press.

[2] M. I. GROSSMAN and C. R. ROBERTSON, Proc. Soc. Exper. Biol. & Med. *68*, 550 (1948).

Anyhow, one can conceive another explanation, namely that the condition (permeability ?) of the gastric secreting cells is altered by the action of Tween 20, and then Benadryl is capable of blocking the histamine effect within the gastric glandular cells. Starting from this assumption the author made some experiments on anæsthetized dogs with pouches of the entire stomach. Tween 20 was administrated intravenously by continuous injection at a rate of about 1 mg/kg/hr. After about 20–30 minutes the gastric secretion started, reached a maximum, but then disappeared in about one hour. Without stopping the administration of Tween, histamine was then given intravenously by continuous injection. When the gastric secretion rate reached a steady state, 0·1 g of Antasten (2 *N* phenylbenzylaminomethyl imidazoline) was given intravenously in massive dose. In all experiments the secretion immediately decreased to 35–50 p.c. of the steady state value. In about 30 minutes the secretion rate again rose to the preceeding value. A second injection of Antasten gave the same effect.

To throw light upon the role of the histamine as a normal gastric secretagogue, experiments were made in which gastric secretion was induced by electrical stimulation of the vagi in the neck *ad modum* VINEBERG[1]. When simultaneously with the nerval stimulation Tween was injected as above, Antasten almost completely blocked the gastric secretion. In about 30 minutes the secretion returned to the preceeding value. The experiments indicate, that the acidity is much more influenced than the peptic activity. Without Tween no inhibition by Antasten was achieved neither in histamine—nor in vagus—stimulated gastric secretion. On cats, attempts in producing gastric secretion by Tween 20 or blocking the histamine-induced secretion by Antasten during Tween-administration have been unsuccessful so far.

SVEN LINDE

Institute of Physiology, University of Uppsala, Sweden, March 5, 1949.

Zusammenfassung

Nach Vorbehandlung mit dem benetzenden Mittel Tween 20 gelang es, sowohl die durch Histaminwirkung als auch durch Vagusreizung erzeugte Magensaftsekretion mit dem Antihistaminpräparat Antasten zu hemmen. Ohne Vorbehandlung mit Tween 20 wird keine Hemmung durch das Antihistaminpräparat hervorgerufen. Es ist möglich, daß Tween 20 die Permeabilitätsverhältnisse in den magensaftsezernierenden Zellen verändert, so daß Antasten die Histaminwirkung in den Zellen selbst blockieren kann.

[1] A. M. VINEBERG, Amer. J. Physiol. *96*, 363 (1931).

Sur un comportement singulier de la L(—)-phénylalanine en présence d'extraits testiculaires

On oppose depuis KREBS[1] les D-acidaminodéhydrases largement répandues, faciles à extraire des tissus à l'aide des solutions salines, aux L-acidaminodéhydrases moins actives et d'extraction beaucoup plus malaisée[2].

[1] H. KREBS, Z. physiol. Chem. *217*, 191 (1933).

[2] M. POLONOVSKI et P. BOULANGER, Bull. Soc. Chim. Biol. *20* 1298 (1938).