

The experimental animals used were mice which were kept on various protein deficient diets. It could be shown that they developed signs of "protein deficiency" (loss of weight, anorexia, decrease of plasma proteins, fatty infiltration in the liver) much more rapidly than rats. In addition such animals excreted a standard water load at a lower rate than normals after only 6 to 7 days on the deficient diets: For example in a series of mice kept on a diet poor in protein and choline (= diet BB; see DICKER¹) the mean volume of urine 90 min after water administration was only 17.5 per cent of that of the control series. When adequate amounts of choline were added to this diet (= diet BC) the mean urine volume rose to 47.4 per cent of that of the controls. A protein deficient vegetable diet (= TT) containing ample choline (DICKER, HELLER, and HEWER³), given to a third group of mice, lowered the mean urine volume excreted during 90 min to 33.2 per cent of the normal.

To study vasopressin inactivation, homogenates of mouse liver mixed with a standard dose of vasopressin and phosphate buffer of pH 6.5 were incubated at 37°C for 30 min. Rats to which water had been administered were injected intraperitoneally with the incubation mixtures and the antidiuretic effect compared with that of known doses of vasopressin. Expressed as percentage of the mean urine volume at 90 min of controls injected with an incubation mixture containing normal mouse liver, the results obtained with livers from animals on the protein deficient diets were as follows:

BB for 7 days = 73.7 per cent,
BB for 10 days = 61.5 per cent,
BC for 7 days = 81.2 per cent,
TT for 10 days = 60.6 per cent.

In other words, it would appear that more antidiuretic material remained active in the liver homogenates from protein deficient animals with the result that the inhibition of water diuresis in the test rats was more pronounced.

Fatty changes in livers of animals kept on the protein deficient diet were investigated by histological and by chemical methods. The histological results are summarized in the table. The chemical estimation of total liver lipids were in reasonable agreement with the histological findings. There would appear to be no parallelism between the results of the diuresis and inactivation experiments, and the intensity of fatty changes: Mice kept on diet TT for 10 days for instance showed a pronounced inhibition of water diuresis and their livers inactivated vasopressin less efficiently, even though no fatty changes could be found in the liver.

Assessment by histological methods of the intensity of fatty changes in the liver of mice on protein deficient diets. The degree of fatty vacuolation is recorded as 0, +, ++, +++ or ++++.

Days on Diet	Control Diet	Diet BB	Diet BC	Diet TT
1	0	+	0	0
2 to 3	0	+++	++	+
4 to 5	0	++++	+++	+
6 to 7	0	++++	no data	++
8	0	+++	+	+
10	0	++	+	0

In view of the findings of LESLIE and RALLI¹ and of DICKER² that the urine of rats fed on a protein deficient diet contained amounts of antidiuretic activity which increased the longer the animals remained on the experimental diet, it would be tempting to associate the lack of the renal response to water in protein deficient mice with the decreased ability of their liver to inactivate vasopressin. However, such an association can at present, for several reasons, be regarded as no more than an inviting possibility.

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Department of Pharmacology, University of Bristol, October 22, 1951.

Zusammenfassung

Mäuse, die auf eiweißarme Kost gesetzt werden, zeigen wenige Tage später eine bedeutende Abnahme ihrer Fähigkeit zur Wasserdiurese. Die Leber solcher Tiere inaktiviert Vasopressin langsamer als Leberbrei von Kontrollen. Ein kausaler Zusammenhang zwischen diesen Befunden ist fraglich. Je nach der Zusammensetzung der eiweißarmen Kost (Cholingehalt, Kalorienwert) und der Versuchsdauer traten bei den Versuchstieren verschiedene Grade von Leberverfettung auf. Diuresehemmung und Verlangsamung der Vasopressininaktivierung konnten jedoch auch in Tieren nachgewiesen werden, deren Leber keinen erhöhten Fettgehalt aufwies.

¹ S. H. LESLIE and E. P. RALLI, *Endocrinology* 41, 1 (1947).

² S. E. DICKER, *Biochem. J.* 46, 53 (1950).

Antidiuretic Action of Small Doses of Enteramine Extracts in the Rat

Extracts of Posterior Salivary Glands of Octopus vulgaris

Alcohol and acetone extracts of posterior salivary glands of *Octopus vulgaris* and *Eledone moschata* inhibit diuresis in rats and in various other mammals, including humans. The antidiuretic action is due to enteramine.

Results obtained in dogs and rats with massive doses of salivary extract were reported in previous communications¹.

The purpose of present researches was to establish:

(a) the smallest dose of salivary extract of *Octopus vulgaris* still active on the diuresis of hydrated rats;

(b) the mechanism of action of small doses of salivary extract. In this connection it was important, above all, to confirm what had already been observed in dogs when using large doses of the same material.

The experiments were carried out on 560 adult albino rats of both sexes, weighing from 130 to 250 g. A first load of tepid tap water (2.5 cm³/100 g) was administered in the morning by stomach tube to fasting animals. After three hours a second water load (5 cm³/100 g) was given and, at the same time, the rats were injected subcutaneously with 1 cm³/100 g distilled water, in which, besides the salivary material (lacking, of course, in the controls), 50 mg sodium thiosulphate (500 mg/kg) and 5 mg *p*-aminohippuric acid (PAH, 50 mg/kg) were dissolved.

¹ V. ERSFAMER and A. OTTOLENGHI, *Exper.* 6, 428 (1950), 7, 191 (1951).

¹ S. E. DICKER, *Biochem. J.* 46, 53 (1950).

Table I

	Percent excretion after				
	1	1½	2	3	7 hours
<i>Water</i>					
Controls	37.9	57.2	68.7	76.7	110.0
Vulgaris 0.002 g/100 g	29.7	50.7	61.9	74.2	103.0
Vulgaris 0.01 g/100 g	25.6	45.9	58.2	71.2	101.7
Vulgaris 0.1 g/100 g	19.4	36.7	48.9	62.8	97.5
<i>Thiosulphate</i>					
Controls	31.3	36.1	38.2	39.4	40.9
Vulgaris 0.002 g/100 g	28.4	35.6	37.2	39.1	40.0
Vulgaris 0.01 g/100 g	26.3	35.0	37.2	39.1	40.3
Vulgaris 0.1 g/100 g	23.4	33.3	36.6	38.2	39.6
<i>PAH</i>					
Controls	62.3	70.7	74.6	77.2	80.0
Vulgaris 0.002 g/100 g	55.8	70.1	73.7	76.2	78.7
Vulgaris 0.01 g/100 g	51.4	67.3	71.9	76.7	79.3
Vulgaris 0.1 g/100 g	44.7	63.1	69.7	73.5	76.3

The animals were placed, in groups of four, into diuresis cages, and urine collected into graduated cylinders and measured, at regular intervals, up to the 7th hour. Thiosulphate and PAH were estimated in samples of urine by the usual methods.

Altogether 140 animals were employed as controls; three other groups, of 140 animals each, were injected with the extract corresponding to 0.002 g, 0.01 g, and 0.1 g fresh salivary tissue/100 g body weight.

At this point it seems worth remembering that the salivary extract obtained from 1 g fresh tissue leaves a dry residue of 40–50 mg, including fats, and that the acute toxicity of the salivary material is remarkably low, corresponding, by subcutaneous route, to about 10 g fresh tissue/100 g rat.

It follows that the doses of extract injected by us represent only 1/5000, 1/1000 and 1/100 of the lethal dose.

The results of our experiments are set down in tables I and II.

Table I gives the percent excretion of administered water and test substances (thiosulphate and PAH); table II, clearly inferred from the preceding, shows the relative percent excretion of water and test substances

when considering as 100 the excretion of the control group.

The experimental methods used in the present investigation (PAH and thiosulphate in the blood were not tested) allow us to measure only the urine flow. As regards glomerular filtration rate and effective renal plasma flow, we have to be satisfied with relative information resulting from the comparison of PAH and thiosulphate excretion values in treated and in control animals.

In the work *in extenso*, results obtained with our procedure will be subjected to criticism and treated statistically. Provisionally we may consider acceptable, also from a quantitative point of view, the information given by the test substances when the amount of such substances excreted during the whole observation period by rats injected with the salivary extract do not differ more than 10–20% from that excreted by control animals.

Even proceeding cautiously, the following conclusions may be drawn from the data reported in the tables:

(1) A significant inhibition of diuresis may be observed in rats after injecting subcutaneously the extract obtained from as little as 2 mg fresh salivary tissue per 100 g body weight. Researches in progress

Table II

	Relative percent excretion (controls = 100) after				
	1	1½	2	3	7 hours
<i>Water</i>					
Vulgaris 0.002 g/100 g	78.3	88.6	90.1	96.7	93.6
Vulgaris 0.01 g/100 g	67.5	80.2	84.7	92.8	92.4
Vulgaris 0.1 g/100 g	51.2	64.2	71.2	81.9	88.6
<i>Thiosulfate</i>					
Vulgaris 0.002 g/100 g	90.7	98.6	97.4	99.2	97.8
Vulgaris 0.01 g/100 g	84.0	96.9	97.4	99.2	98.5
Vulgaris 0.1 g/100 g	74.8	92.2	95.8	96.9	96.8
<i>PAH</i>					
Vulgaris 0.002 g/100 g	89.6	99.1	98.8	98.7	98.4
Vulgaris 0.01 g/100 g	82.5	95.2	96.4	99.3	99.1
Vulgaris 0.1 g/100 g	71.7	89.2	93.4	95.2	95.4

having proved that the amount of pure enteramine contained in the fresh salivary tissue is about $10^{10}/_{00}$, one may deduce that $2 \mu\text{g}$ enteramine/100 g rat are certainly effective.

(2) The reduction of diuresis is accompanied by a sure, though less marked reduction of thiosulphate excretion and by a similar reduction of PAH excretion.

The decrease of thiosulphate excretion demonstrates that enteramine antidiuresis must be considered, at least to the greater part, as a consequence of a diminished glomerular filtration, which in its turn is clearly caused by a drop in intraglomerular hydrostatic pressure.

(3) At our dosage, the salivary extract is quite ineffective on the systemic blood pressure of the rat. The fall of intraglomerular pressure and the slowing of blood flow through the intertubular capillary network, as indicated by the lowering of PAH excretion, can therefore only be explained by a constriction of the *afferent vascular bed* of the glomerulus.

Researches now in progress aim to ascertain with greater accuracy the point of attack of enteramine and the modifications in intrarenal circulation caused by the substance. At present it is enough to have gained confirmation that small doses of salivary material act on rats by a mechanism exactly similar to that observed in dogs after administration of massive doses.

It must be pointed out that salivary extracts of *Octopus vulgaris* by no means represent the most suitable

material for studying the antidiuretic action of enteramine.

Indeed they contain, besides enteramine, also tyramine and octopamine (= *l-norsynephrine*), both possessing a marked diuretic activity due to their systemic hypertensive action and their constricting action on the *efferent* vascular section of the glomerulus.

Results achieved in the present investigation have been conclusively confirmed using extracts of *Discoglossus pictus* skin, which is just as rich in enteramine as salivary extracts of *Octopus vulgaris* but free of disturbing substances, as well as using pure enteramine and synthetic enteramine-like products.

V. ERSPAMER and A. OTTOLENGHI

Pharmacological Institute, University of Bari, September 3, 1951.

Zusammenfassung

Die kleinste Dosis der Speicheldrüsenextrakte von *Octopus vulgaris*, die bei der Ratte noch sicher diuresehemmend wirkt, entspricht 2 mg frischem Gewebe pro 100 g Tier.

Die antidiuretische Wirkung ist einer Drosselung des afferenten Gefäßsystems des Glomerulus zuzuschreiben, mit nachfolgender Verminderung des hydrostatischen intraglomerularen Druckes und der Durchströmung des intertubularen Kapillarnetzes.

Nouveaux livres - Buchbesprechungen - Recensioni - Reviews

Grating Spectrum of Iron

By A. GATTERER

(Specola Vaticana, Città del Vaticano 1951) (\$25.-)

Der Leiter des spektrochemischen Laboratoriums der Vatikansternwarte hat mit der Neuherausgabe dieses Atlases des Eisenspektrums die vatikanischen Prachtwerke, welche die optischen Spektren zur Darstellung bringen, um eines vermehrt, das, indem es das Standardspektrum enthält, von ganz besonderem Nutzen ist. Auf 45 Originalphotoabzügen von 23×30 cm Größe ist das Eisenspektrum mit der konstanten Dispersion von $0,7 \text{ \AA/mm}$ nach Aufnahmen mit einem 21-foot-Gitterspektrographen von Jarell-Ash Co. dargestellt, und zwar das Bogenspektrum im Bereich $\lambda\lambda 8900-2150$ und das Funkenspektrum zwischen $\lambda\lambda 5300-2150$, ferner im Gebiet $\lambda\lambda 8900-5300$ das Spektrum des Zirkonbogens, dessen zahlreiche Linien und ZrO-Banden in glücklicher Weise die Lücken des Eisenspektrums überbrücken. Die Wahl von Zirkon wird mit dem astrophysikalischen Interesse dieses Elementes begründet. Auf zwei Tafeln ist mit der Dispersion von $2 \text{ \AA/mm}$ das Neonspektrum zusammen mit den Eisenlinien im Bereich $\lambda\lambda 8900-5900$ wiedergegeben.

Sämtliche Linien sind auf das sorgfältigste mit 6- bis 7-ziffrigen Wellenlängenangaben, kritisch nach den besten Quellen gesichtet, angeschrieben. Das Werk ist aufs beste geeignet, den Spektroskopikern, welche mit den modernen Spektrographen arbeiten, die rasche Identifizierung von Spektrallinien ohne mühsame Aus-

messung zu ermöglichen, und es ist sicherlich dank der beispiellosen Sorgfalt, mit der es hergestellt ist, schlechthin unübertreffbar.

E. MIESCHER

Einführung in die chemische Thermodynamik

VON GUSTAV KORTÜM

303 Seiten mit 85 Abbildungen

(Vandenhoeck & Ruprecht, Göttingen 1949)

(Kart. DM 17.80, geb. DM 20.-, Leinen DM 22.-)

Das neue Werk des bekannten Autors zeigt zunächst den «klassischen» Aufbau eines Thermodynamik-Buches; in sieben Kapiteln werden behandelt: Definitionen und Grundbegriffe, die thermische Zustandsgleichung, der 1. Hauptsatz, der 2. Hauptsatz, das thermische Gleichgewicht, der Nernstsche Wärmesatz, die Thermodynamik der Phasengrenzflächen.

Bemerkenswert und sehr erfreulich ist die Art der Darstellung im einzelnen; sehr konsequent wird der Leitgedanke durchgeführt, nämlich den Leser mit der begrifflichen und mathematischen Technik der thermodynamischen Behandlung chemischer Probleme vertraut zu machen. Erreicht wird diese Geschlossenheit durch Verzicht auf alles Beiwerk; mit Recht wird ein übermäßiges Eingehen auf Grundlagenfragen, werden mathematische Weiterungen, ebenso größere Abschweifungen in das Gebiet der molekularen Deutung vermieden. Nach Durcharbeiten des Werkes sollte der Leser, insbesondere der Studierende der Chemie, imstande