## Antidiuretic Action of Enteramine

Previous investigations[1] have shown that acetone extracts of posterior salivary glands of *Octopus vulgaris* and *Eledone* (*E. moschata* and *E. Aldrovandi*) contain a principle which markedly reduces the diuresis of hydrated rats.

Later and more extensive researches, which will be reported in detail in future papers, have confirmed these first observations, allowing us to individualize and characterize the antidiuretic principle more accurately.

This is now to be identified, with reasonable certainty, as the enteramine-like substance which for several years has been known to exist in the posterior salivary glands of the *Octopoda* mentioned above. In fact:

(1) The field of distribution of the antidiuretic principle strikingly covers that of enteramine (or enteramine-like substances), both in the different animal species and in the different organs of an individual animal. Indeed, not only extracts of salivary glands of *Octopus vulgaris* and *Eledone* possess antidiuretic activity, but also extracts of the hypobranchial body of *Murex trunculus* and *Murex brandaris*, as well as, although to a lesser extent, extracts from ox spleen, gastric mucosa of rabbits and dogs, and duodenal mucosa of oxen and dogs. Extracts of hepato-pancreas, kidney, gill, intestine, ovary, testicle, tentacle muscle and hemolymph of *Eledone moschata* and *Octopus vulgaris* have practically no antidiuretic action (only in massive doses can they reduce or delay the urine excretion). Extracts from kidney, liver, brain, testicle, lung, heart, skeletal muscle and smooth muscle of the stomach and intestine of a calf, and extracts from the smooth gastro-intestinal muscle of a dog are equally ineffective.

It has already been pointed out in the preceding communication that extracts of posterior salivary glands of *Octopus macropus*, which are completely free of enteramine, exhibit an evident stimulating action on diuresis instead of an antidiuretic action.

(2) Provided that care has been taken to eliminate any possible interfering materials (murexine and moschatine, for example), the antidiuretic activity of enteraminic extracts is roughly but clearly proportional, both in intensity and duration, to the content of enteramine, as determined colorimetrically (coupling reaction with diazonium salts in an acid medium, iodine reaction) and biologically (œstrus-uterus of rats or mice, urinary bladder of dogs).

(3) Any procedure which destroys or inactivates enteramine (treatment with formalin, with diazonium salts, with potassium iodate, benzoylation, methylation, ultraviolet irradiation[2]) also destroys the antidiuretic activity of the enteramine-containing extracts. Moreover, the antidiuretic principle of crude extracts closely resembles enteramine in its resistance to alkali and acids in the heat.

Enteraminase (amine oxidase) of fresh phosphate extracts of the intestine, liver or kidney of a guinea-pig completely destroys the antidiuretic activity of the enteraminic extracts, at least so long as the enzyme is not inhibited by methylene blue.

(4) On fractionating dry residues of salivary extracts of *Octopus vulgaris* by various methods, the antidiuretic activity always follows the distribution of the enteramine-like substance. So, for instance, in chromatographic partition experiments on paper[1] and columns, only the eluates from enteraminic spots and zones show diuresis inhibition.

The antidiuretic activity of enteramine-containing extracts has so far been established in rats (the animals on which the bulk of our experiments has been carried out), dogs, guinea-pigs, frogs, toads and humans, both healthy and suffering from diabetes insipidus. Rabbits have given inconclusive results.

Doses of salivary extracts of *Octopus vulgaris*, corresponding to 0·2–0·5 g fresh tissue per kg body weight, have been proved definitely effective in rats and humans.

The onset of action is almost immediate (a few minutes after the s. c. or i. m. injection of enteraminic extracts was given). The urinary block may be total, and lasts for a variable time (up to 5–6 hours or more); it is approximately proportional to the amount of antidiuretic extract injected, naturally within certain limits.

Enteramine inhibits and reduces not only normal and water diuresis, but also that due to xanthines, mercurials, salts and urea.

The hitherto tested enteramine-containing extracts have been numerous and partly obtained from very rich material (about 15,000 specimens of *Octopus vulgaris*, at least as many of *Eledone*, and more than 10,000 specimens of *Murex trunculus*).

Our experiments have been conducted on more than 500 groups of 4–5 rats.

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V. ERSPAMER and A. OTTOLENGHI

Pharmacological Institute, University of Bari, July 20, 1950.

*Zusammenfassung*

Acetonextrakte der hinteren Speicheldrüsen von *Octopus vulgaris* und *Eledone* (*E. moschata* und *E. Aldrovandi*), der Hypobranchialdrüse von *Murex trunculus* und *Murex brandaris*, sowie der Milz und der Magen- und Dünndarmschleimhaut von Säugetieren verhindern merkwürdigerweise die Diurese der Ratte, des Hundes, des Meerschweinchens, des Frosches, der Kröte und des Menschen (gesund und krank an *Diabetes insipidus*).

Die diuresehemmende Wirkung solcher Extrakte ist ausschließlich ihrem Enteramingehalt zuzuschreiben.

Enteramin hemmt nicht nur die normale und die Wasserdiurese, sondern auch die durch Salze, Xanthinderivate und Quecksilberverbindungen erzeugte Diurese.

[1] V. ERSPAMER and G. BORETTI, Exper. *6*, 348 (1950).

[1] V. ERSPAMER e L. PEROSA, Exper. *4*, 486 (1948).

[2] V. ERSPAMER Arch. Sci. Biol. (Ital.) 20, 296 (1940); Acta pharmacol. *4*, 213 (1948).

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## The Effect of Aureomycin on Tissue Cultures

One of the most important of the new antibiotics described in the past few years is aureomycin, which has been isolated from the substrate of *Streptomyces aureofaciens*[1]. The antibiotic has been used mainly in the form of its crystalline golden-yellow hydrochloride, which is soluble in water, but somewhat less soluble in saline. The dilute solutions quickly lose their activity at room temperature and alkaline $p_H$. Human serum also seemed to have an inhibiting effect on the antibiotic activity[2].

[1] B. M. DUGGAR, Ann. N. Y. Acad. Sci. *51*, 177 (1948).

[2] T. F. PAINE, J. Bact. *56*, 489 (1948).