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THE PRESENCE IN ERGOT AND PHYSIOLOGICAL ACTIVITY OF β-IMIDAZOLYLETHYLAMINE

(Preliminary Communication)

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(*Reprinted from the "Journal of Physiology,"* Vol. xl, June 18, 1910)

From
THE WELLCOME PHYSIOLOGICAL RESEARCH LABORATORIES
BROCKWELL HALL
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LONDON, S.E.

Journal Physiology, Vol. XL.
[*From the Proceedings of the Physiological Society*, June 18, 1910.]

The presence in ergot and physiological activity of β-imidazolylethylamine. By G. Barger and H. H. Dale. (*Preliminary communication*[1].)

Three physiological actions have been used as indices of the therapeutic value of ergot and its extracts.

(1) Production of gangrene of the cock's comb.
(2) Production of a rise of arterial blood-pressure.
(3) Stimulation of the isolated uterus to tonic contraction—preferably the uterus of the non-pregnant cat (Kehrer)[2].

In previous communications we have shown that (1) is due to the specific alkaloid ergotoxine, which has been found only in ergot, and which causes contraction of various plain-muscular organs, followed by the selective paralysis of motor sympathetic effects described by one of us. We showed also that (2) is due not only to ergotoxine, but often in much larger degree to the presence of *p*-hydroxyphenylethylamine, which is not specific to ergot, being produced also by the action of various micro-organisms on tyrosine.

P-hydroxyphenylethylamine, which resembles adrenine in the type of its action, causes relaxation of the non-pregnant cat's uterus: ergotoxine has but little effect on it when it is treated as an isolated organ. It was clear that the production of (3) by some specimens of ergot extracts in very small doses must be due to the presence of a third active principle.

As Kehrer found, extracts of ergot vary widely in their action on the uterus, as measured by his method, the *ergotinum dialysatum* of Wernich being especially active. Dialysis in itself does not alter the activity, and it occurred to us that the growth of micro-organisms during dialysis might account for the high degree of activity of the dialysed preparation. This supposition we confirmed by experiment. We further found that a like activity was possessed by commercial extracts of meat and of yeast, so that the third active principle, like *p*-hydroxyphenylethylamine, was a substance not peculiar to ergot, and produced by putrefaction as well as by the ergot-fungus..

[1] See also *Proc. Chem. Soc.* xxvi. p. 128, 1910.
[2] *Arch. f. exp. Path. u. Pharmakol.* lviii. p. 366, 1908.

Applying Kutscher's[1] silver method to a specimen of *ergotinum dialysatum* we succeeded in isolating a few centigrammes of the picrate of an intensely active base, which produced the characteristic action on the cat's non-pregnant uterus in minute doses. Its action, the details of which will be published later, further differs from that of the other active principles in that it causes a fall of systemic arterial pressure when injected intravenously. The manner in which the base was precipitated by silver and by mercury suggested a relation to histidine, which was further made probable by the fact that the base gave Pauly's colour-reaction with diazobenzenesulphonic acid. Pure histidine was found to be inactive, but acquired the characteristic activity on putrefaction. It therefore seemed probable that the base was β-imidazolylethylamine, produced from histidine by splitting off carbon dioxide. We have been able to confirm this identification through the kindness of Dr D. Ackermann, who forwarded to us a specimen of the di-picrate of β-imidazolylethylamine, which he recently obtained by the putrefaction of histidine[2]. This was found to be in all respects identical with the picrate obtained by us from the ergot extract.

NOTE. Since the above was forwarded for publication a paper by Kutscher (*Centralbl. f. Physiol.* XXIV. p. 163) has come to our notice. Kutscher describes the isolation from ergot of the picrolonate of a base which was intensely toxic, and which chemically had the characteristics of β-imidazolylethylamine. He found, however, that the latter substance, as prepared by Ackermann, had a different physiological action. Without expressing any opinion as to the identity of the base obtained by Kutscher, we think it desirable to state that the base obtained by us from ergot agreed with that kindly furnished by Dr Ackermann, not only in chemical characters, but in all points of physiological action with regard to which we compared them.

[1] *Zeitschr. Nahr. Genussm.* x. p. 528, 1905.
[2] *Zeitschr. f. Physiol. Chem.* LXV. p. 504, 1910.