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A THIRD ACTIVE PRINCIPLE IN ERGOT EXTRACTS

(Preliminary Note)

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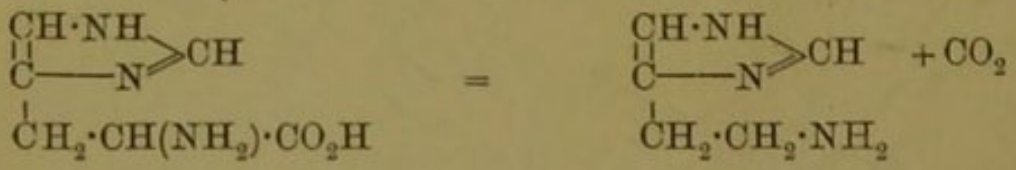
***133. "A third active principle in ergot extracts." (Preliminary note.) By George Barger and Henry Hallett Dale.**

In addition to the active principles previously described by the authors as present in ergot and its extracts, namely, ergotoxine (*Trans.*, 1907, **91**, 337; *Biochem. J.*, 1907, **2**, 286) and *p*-hydroxyphenylethylamine (*J. Physiol.*, 1909, **38**, lxxvii; *Trans.*, 1909, **95**, 1123), there remained for identification the substance responsible for the intense activity exhibited by some ergot extracts in producing contraction of the isolated, *non-pregnant* uterus of the cat (compare Kehrer, *Arch. exp. Path. Pharm.*, 1908, **58**, 366).

As Kehrer found, this action is specially characteristic of Wernich's *Ergotinum dialysatum*. The relative abundance of this principle in dialysed extracts suggested that it was wholly or partly produced by micro-organisms, and this supposition was confirmed by physio-

logical experiment. It was also found that commercial extracts of meat and of yeast have a similar activity in smaller degree. Applying Kutscher's method (*Zeitsch. Nahr. Genussm.*, 1905, **10**, 528; 1906, **11**, 582) for separating bases from meat-extract, the authors obtained the active principle from ergotinum dialysatum as a silver compound by adding silver nitrate in excess and then baryta. The hydrochloride of the physiologically active base, obtained from this silver precipitate, is readily soluble in cold methyl alcohol, less so in hot ethyl alcohol, and very sparingly so in cold ethyl alcohol. After suitable purification, a minute quantity of a crystalline picrate, melting at 220—230°, and a picrolonate, very sparingly soluble in boiling water and melting at about 250°, were obtained. The base regenerated from either salt had an intense action on the uterus, and gave Pauly's reaction with *p*-diazobenzenesulphonic acid. This, together with the conditions under which the base was precipitated by baryta in the presence of silver nitrate, suggested that it was a derivative of histidine. Histidine itself was found to be inactive, but acquired a trace of activity on heating, and became markedly so when exposed to putrefaction. It therefore seemed probable that the active base was β-iminazolylethylamine, produced from histidine



by loss of carbon dioxide in the same way that *p*-hydroxyphenylethylamine in ergot extracts is produced from tyrosine.

This provisional identification is supported by the fact that the properties of the hydrochloride, picrate, and picrolonate above described correspond closely with those of the salts of β-iminazolylethylamine synthesised by Windaus and Vogt (*Ber.*, 1907, **40**, 369), and quite recently obtained by Ackermann (*Zeitsch. physiol. Chem.*, 1910, **65**, 504) by the putrefaction of histidine.*

* Dr. Ackermann's kindness, which the authors gratefully acknowledge, has since enabled them to complete the identification by direct comparison of the base from ergot with that which he obtained by the putrefaction of histidine. In the crystalline form of their picrates, and particularly in their action on the uterus, the two bases were found to be identical.

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