

The values for the elementary analysis (C=71.46; H=7.38; N=11.66 per cent.) communicated by the English investigators in March, 1935,<sup>11</sup> as they say with reservation, differ so much from the theory of our ergobasine formula  $C_{19}H_{23}O_2N_3$  (C=70.11; H=7.13; N=12.92 per cent.) that every chemist must conclude that Dudley and Moir analyzed either another or an impure substance.

H. H. Dale seems to have overlooked that in the report on Ergobasine, under the chapter, "Préparation de l'Ergobasine"<sup>12</sup> two methods for preparing ergobasine are given, which are based on the very slight solubility of the alkaloid in chloroform and its good solubility in water. These properties made possible the separation of ergobasine from the alkaloids of the ergotamine-ergotoxine group. Since then H. W. Dudley<sup>13</sup> also published a method for the preparation of ergometrine, but even here are missing the analyses of the base and its salts and the exact measurement of the optical rotation which would enable the chemist to identify the prepared substance. Ergometrine is now reported to be dextro-rotatory in ethyl alcohol. Only in a paper presented by C. Moir<sup>14</sup> we find the statement that ergometrine has, according to the investigation of H. W. Dudley, the formula  $C_{19}H_{23}O_2N_3$ , which is the same as we have found for ergobasine.

The data published so far on the identity of the substances prepared in different laboratories are briefly as follows:

W. A. Jacobs and L. C. Craig<sup>15</sup> have shown by direct comparison that the substance isolated by them from ergot of rye is identical with ergobasine. The independent analyses made by these authors confirm the formula  $C_{19}H_{23}O_2N_3$  for ergobasine. The successful cleavage to lysergic acid and 2-aminopropanol-1 constitutes additional and valuable evidence for the formula, proving at the same time the connection between ergobasine and the alkaloids of the ergotamine-ergotoxine group.

A sample of 40 mgs ergostetrine, which Professor Thompson kindly sent us a few weeks ago in exchange for ergobasine, showed in crystalline form, water solubility and optical rotation in water ( $[\alpha]_D^{20} = +88.5^\circ$ ) the characteristics of ergobasine. Ergostetrine is therefore in all probability identical with ergobasine.

We have obtained from a trade package of ergometrine, of an English firm, an alkaloid preparation which was not homogeneous, but from which a fair amount of pure ergobasine was isolated.

The analyses reported by M. S. Kharasch and R. R.

Legault<sup>16</sup> concerning their substance differ considerably from our ergobasine analyses and led to the formula  $C_{21}H_{27}O_3N_3$  for ergotocin. The description of ergotocin as given by these authors differs from the published data on ergobasine, for instance, in the difficulties in salt formation of ergotocin with monobasic acids. Exact and direct comparison is still lacking. We did not fail to place a sufficient quantity of pure ergobasine for comparison purposes at the disposal of all the investigators who desired it.

That ergot of rye contains not only one alkaloid but several with the approximate molecular weight of ergobasine is shown by a recent communication of S. Smith and G. M. Timmis,<sup>17</sup> which describes the isolation of a new ergot alkaloid characterized by its decomposition point at  $195^\circ$ , its salt formation with  $HNO_3$ ,  $HBr$ , and  $H_2SO_4$  and by the very high optical rotation  $[\alpha]_{5461}^{20} = +520^\circ$  ( $c=1$  in chloroform). The new substance named ergometrine, with the formula  $C_{19}H_{23}O_2N_3$ , proved to be isomeric with ergobasine (ergometrine) and could be transformed into ergometrine. The newly discovered alkaloids seem to be a group of substances like the long known alkaloids of ergot, ergotinine-ergotoxine and ergotamine-ergotaminine, which are similar as a group, but possess different individual characteristics.

Through the exact physiological and chemical comparison of ergotoxine and ergotamine, we know that the chemical identity of substances can not be determined from the similarity of physiological action. For many years ergotoxine and ergotamine were supposed to be pharmacologically identical, and it is only recently that especially E. Rothlin<sup>18</sup> has shown some qualitative differences in the minute pharmacological activity of these alkaloids. Chemically, the difference of the two alkaloids was always evident.

The decision on the question of identity or difference of the newly prepared alkaloidal substances isolated by various investigators can of course only be determined by exact physical and chemical comparison.

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#### HETEROTHALLISM OF SUNFLOWER POWDERY MILDEW

THE formation of perithecia on only certain areas of diseased leaves and at the intersection of two mildew colonies indicated the likelihood of heterothallism of *Erysiphe cichoracearum* D.C. on sunflower, *Helianthus annuus* L. The formation of perithecia on young excised leaves floating on 5 per cent. sucrose solution

<sup>11</sup> *Brit. Med. Jour.*, No. 3871, p. 521, 1935.

<sup>12</sup> *Bull. Sci. Pharmacol.*, 42: 259, 1935.

<sup>13</sup> *The Pharmaceutical Journal*, June 15, 1935.

<sup>14</sup> *Brit. Med. Jour.*, No. 3890, p. 178, July 27, 1935.

<sup>15</sup> *SCIENCE*, 82: 16, 1935.

<sup>16</sup> *Jour. Am. Chem. Soc.*, 57: 956 and 1140, 1935.

<sup>17</sup> *Nature*, August 17, 1935, p. 295.

<sup>18</sup> E. Rothlin, *Archivio di Scienze Biologiche*, 18: 1-4, 1933, and *Klin. Wsch.*, 12: 25, 1933.

in petri-dish moist chambers at room temperature indicated that four of the conditions commonly cited as favoring perithecium formation, namely, old leaves, a host in a low state of nutrition, a dry atmosphere and low temperature, did not satisfactorily account for the formation of perithecia in this case. Fifteen single conidium cultures were isolated and maintained on excised sunflower leaves on sucrose solution. One of these single spore cultures has been maintained for over four months and all of them for six weeks or more under various cultural conditions without showing any tendency towards perithecium formation. Various combinations of these cultures were made, and perithecia were formed when certain cultures were combined. Two single conidium cultures, 1 and 1A2, which formed perithecia on combining, were studied in more detail. In two out of three tests with excised leaves floating on sucrose solution, and in three out of three tests with excised leaves with their petioles in flasks of mineral nutrient solution, perithecia were formed, though rather sparsely in most tests, when sunflower leaves were inoculated at the same place with both cultures. In one test, all twelve inoculations with culture 1 alone, and all 12 inoculations with culture 1A2 alone, formed conidia only, while seventeen out of twenty inoculations with the two cultures together formed perithecia in addition to conidia. This is considered to be reasonable proof of heterothallism in *Erysiphe cichoracearum* and is believed to be the first record of heterothallism in the *Erysiphaceae*. Cytological studies of the phenomenon are being conducted by Dr. Ruth Allen.

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### RARE AQUATIC PHENOMENA

THE early morning of August 1 saw the beginning of an occurrence that, so far as the writer can find out, has never happened in this part of the country before, and is only recorded in a very few places throughout the world during the past fifty years or more.

About 18 miles north of New Haven, Connecticut, between the towns of Wallingford and Meriden, is a small lake known as the "North Farms reservoir." It is not over fifty feet above sea level; the surface area is between 125 and 150 acres, and it receives the drainage from a small basin of not over one square mile in extent. The lake has no inlet; it is spring-fed and very shallow, being only 8 feet deep in the deepest part, with an average mean depth of about 4 feet. The bottom is mostly mud and very full of weeds.

On the morning of August 1 the writer was called

on the phone by Mr. S. R. MacDonald, a fruit grower whose property borders on the lake, and was told that "the whole surface of the lake was covered with fish of all kinds and sizes, that were breaking water incessantly, and that many of them were dead and dying." It took only a few minutes to reach the lake, and the sight was one never to be forgotten. Literally every square foot of the surface had one or more fish trying to breathe with their noses out of water. The fish consisted of pickerel, perch, calico bass, bullheads, sunfish and pond shiners.

Shortly after noon the fish were dying by the thousand and sinking to the bottom, while those that had been the first to die, probably during the night before, began to rise to the surface. In the meantime the water began to assume a peculiar milky color that was far from normal.

The shore-line of the lake was thoroughly examined. The vegetation along the shore showed no discoloration, nor any other sign of the action of poison, which every one seemed to suspect was at the bottom of it. In the meantime more and more fish kept coming to the surface and heading for shallow water. In some instances they even swam up on the banks where they were high and dry, and continued flopping around until they died.

Late in the afternoon Dr. Copeland, of the State Board of Water Supply, came down and analyzed the water from samples taken at different depths, all of which showed that practically all the oxygen had been exhausted, barely a trace showing in the analysis. Dr. G. E. Hutchinson, of Yale University, also came up to investigate the phenomena, and the results he obtained coincided with those of Dr. Copeland. A number of fish, both alive and dead, were taken to Professor Charles R. Hoover, of Wesleyan University, who after performing autopsies on the specimens gave as his opinion that the fish had died from a complete lack of oxygen, no trace of copper or other poisonous matter being present.

At the time of the catastrophe the pond had been "working" for several days, while a few days before there had been some severe rains, accompanied by abrupt changes in temperature. It seems that the decaying vegetation washed into the lake by the rains, plus the sudden changes in temperature, caused the sudden decaying of the Algae, which in turn caused a precipitation of decayed vegetable matter that absorbed all the oxygen. This naturally led to the suffocation or drowning of all the fish. It is estimated that over 400,000 fish died, and that not one was left alive. Even the eels and crawfish crawled out on the banks to die.

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