

The Chemical Constitution of Cerebrine. By EDWARD G. GREGGEGAN, M.D., Assistant Medical Officer, Gloucester County Asylum.

To judge from the sparse literature of the subject, cerebrine has not often been chemically studied. The first work of any importance was done by W. Müller.* Müller obtained the body, which he called "Cerebrine," free from phosphorus by digesting the brain with baryta-water. He also analysed it, and proposed the formula, $C_{34}H_{33}NO_6$.

Liebreich† afterwards regarded it as a decomposition product of his "Protagon." But subsequently Diakonow‡ and Hoppe-Seyler§ proved that in all probability protagon was a mere mixture of cerebrine and lecithine. Quite lately Gamgee and Blankenhorn|| have reasserted Liebreich's view.

Distribution of Cerebrine.—Cerebrine is to be found in considerable quantities only in the substance of the brain and nerves, and mainly or exclusively in the white matter.¶ A body which from its reactions may be considered as identical with Müller and Diakonow's cerebrine, was found by Hoppe-Seyler** in pus corpuscles; and I extracted it from the electric organ of the torpedo fish, and from a cancer of the liver. But the quantity in these latter cases was small.

Cerebrine appears to be very resistant to decomposition, as I found it in a brain that had rotted for four months.

Method of obtaining Cerebrine, and its Composition.—The brain is passed through a mincing-machine, and after treatment with cold alcohol and æther, it is boiled in alcohol. The alcohol is filtered off while hot, and the filtrate on cooling deposits crystals of cerebrine impurified by cholesterine and lecithine. The cholesterine is removed by æther, and then the precipitate is boiled with baryta-water, the superfluous baryta precipitated by carbonic acid, and the cerebrine dissolved in hot absolute alcohol, and re-deposited when the alcohol cools. Obtained in this manner, it has all the characteristics described in Hoppe-Seyler's *Handbuch der Physiol. Chemie.* (pp. 195-7).

* Müller, "Ann. der Chem. und Pharm." Band 105, p. 365.

† Virchow's "Archiv." Bd. 39, 1867.

‡ "Centralblatt für die Med. Wiss.," 1868, No. 7.

§ "Med. Chem. Untersuchungen," p. 437.

|| "Journal of Physiology."

¶ Petrowski, "Pfüger's Archiv," viii. 367.

** Loc. cit.

I analysed the body, and obtained the following figures:—

- I.—0.2455 substance gave $\text{CO}_2 = 0.621$ and $\text{H}_2\text{O} = 0.2395$.
 II.—0.1740 substance gave $\text{CO}_2 = 0.439$ $\text{H}_2\text{O} = 0.171$.
 III.—0.1315 substance gave $\text{CO}_2 = 0.332$, $\text{H}_2\text{O} = 0.129$.
 IV.—0.1685 substance gave $\text{CO}_2 = 0.4240$, $\text{H}_2\text{O} = 0.1668$.

And Nitrogen (Dumas' method):—

- I.—0.400 gave N = 0.0057.
 II.—0.367 gave N = 0.0053.

Reduced to percentages:—

	I.	II.	III.	IV.	Average.
C	68.68	68.82	68.84	68.68	68.47
H	10.84	10.90	10.90	11.10	10.90
N	1.42	1.46			1.44

From these figures we may deduce the empirical formula, $\text{C}_{57} \text{H}_{110} \text{N}_3 \text{O}_{25}$ for cerebrine. The quantity of nitrogen is only about a quarter of that found by Müller.

Decomposition products of Cerebrine.—Liebreich* mentions having found a saccharine substance by boiling his protagon with dilute mineral acids. Afterwards Diakonow† broke up cerebrine with sulphuric acid into a saccharine substance which turned polarised light to the left but did not ferment, and other substances which he did not investigate further.

After several experiments on the decomposition of cerebrine with different re-agents, I selected the following method:—

Mix cerebrine in a mortar with concentrated sulphuric acid. At first a clear dark yellow solution is obtained, with a fibrous mass floating on its surface. This mass is at first light brown, but changes to a dark purple, and finally becomes black. The change in colour seems to be due to the attraction of moisture, as I found it did not take place in a dried atmosphere. In mixing, acid fumes in small quantity are developed, probably sulphurous acid. The solution and the floating mass are then brought into about ten times their volume of water, which gives a pinkish and then a white colour to the insoluble substance. The fluid is put on a water bath till the insoluble parts adhere together, and then allowed to cool, and filtered. I shall return presently to the body in solution. The insoluble body it is impossible to obtain quite free from sulphuric acid by filtration, as it swells up when washed, and cannot be further filtered. So I extracted it with æther, distilled off the æther, and boiled the body several times with water till the acid reaction disappeared. During

* Virchow's "Archiv," Bd. 39, 1867.

† Loc. cit.

this process it melts and adheres to the bottom of the vessel, and, on cooling, remains as a hard brittle body.

The substance obtained in this manner, which forms about 0.85 of cerebrine, I have called "cetylid." It is most soluble in chloroform, and easily soluble in æther and hot alcohol. It contains no nitrogen, and I have estimated its melting point to be between 62° and 65° C.

Combustion analyses of the powdered substances, dried at 105° C, give the following results:—

I.—0.210 substance gives	CO ₂ = 0.524,	H ₂ O = 0.2025
II.—0.198 substance gives	CO ₂ = 0.493,	H ₂ O = 0.1970
III.—0.177 substance gives	CO ₂ = 0.4435	H ₂ O = 0.1695.

Or in percentages:—

	C.	H.
I.—	68.05	10.78
II.—	67.97	11.04
III.—	67.92	10.65
Average	67.98	10.81

I then heated the compound cetylid in a platinum crucible with solid caustic potash. But as the mixture threw up such a froth, I introduced the substance with potash into a wide glass tube, one end of which was closed and the other drawn out into a long neck. This tube was then heated in an oil bath, while the neck opened under mercury to collect any gases which might develop. Gas began developing at about 170° C, but was most rapid between 270° and 300°. When the gas bubbles ceased, there was a yellowish white mass in the tube, and a little carbonaceous substance. This was put in water, and the solution extracted with æther. The quantity obtained in this way was very small, and appears to be undecomposed cetylid, as the melting point and solubility agree.

The aqueous solution was next acidulated with hydrochloric acid, and a second time extracted with æther. This time the æther took up a large quantity of the substance. After distilling off the æther, I dissolved the residue in hot alcohol, and let it cool very gradually. In 24 hours I obtained white, leaf-like, twisted crystals. The melting point of these crystals lay between 59.5° and 62° C, and the melted substance began to solidify at 57.5°. The alcoholic solution has a weak acid reaction. The crystals I again dissolved in alcohol, and added carbonate of sodium, evaporated to dryness, extracted with absolute alcohol, filtered, distilled off the alcohol, and dissolved the solid in a little hot water. When cold, the solution formed a firm soap. Adding a little more

water, and heating, by addition of chloride of barium, I converted the sodium compound into the barium salt, and analysed this salt when well washed and dried at 115° C. The melting point, crystallization from alcohol, and the firm gelatinous consistency of the sodium salt, all rendered it highly probable that I had to deal with palmitic acid; and this conjecture was confirmed by the analysis:—

0.169 substance gave H₂O = 0.145 CO₂ = 0.367 and Ba = 0.0355

	Palmitic Acid.	Analysis.
H	9.58 p.c.	9.54 p.c.
C	59.35 "	59.20 "
Ba	21.17 "	21.12 "

In reading through Müller's article a second time, it struck me that a decomposition product, which he obtained by boiling cerebrine with concentrated nitric acid, was very similar to palmitic acid, and on reckoning out his figures I found they agreed exactly with the composition of palmitic acid. Naturally no value could be attached to this result, obtained with nitric acid; and, indeed, Müller does not seem to have entertained any notion of the nature of the substance.

The gases which are developed, when cetylid is melted with potash, consisted of CH₄, 11.44 p.c.; H₂, 50.73 p.c.; N 37.83. From the presence of hydrogen, and the formation of palmitic acid, we may conclude that the alcohol of the palmitic acid, *i.e.*, cetyl alcohol, is contained in cetylid; and further, from development of methane, we might assume that the cetyl alcohol is combined with a hydrocarbon of the composition, say of glycogen (C₆ H₁₀ O₅). This supposition demands 68.89 p.c. C, and 10.88 p.c. H, in cetylid. I found an average of 67.98 p.c. C, and 10.88 p.c. H. The empirical formula would then be C₃₃ H₄₈ O₅.

The decomposition of cetylid into cetyl alcohol and hydrocarbon, and combination of one molecule of water, might be expressed by the equation, C₃₃ H₄₈ O₅ + H₂ O = C₁₆ H₃₄ O (cetyl-alcohol) + C₆ H₁₀ O₅. There is, however, no proof of the presence of a hydrocarbon, further than the development of marsh gas. But on any other supposition it must be shown that such compounds exist, of the same composition as that I found for cetylid; and its decomposition is inexplicable to me on any other supposition than the one I have given.

The formation of palmitic acid from cetyl alcohol is expressed by C₁₆ H₃₄ O + KOH = 2H₂ + C₁₆ H₃₁ KO₂.

With the object of further investigating the constitution of cetylid, I heated it with water in a sealed tube up to

200° C. After eight hours I opened the tube, but there was no pressure of gas. By this means I obtained a substance, which melts at a temperature below 100° C, and a strongly acid, yellowish fluid, which at first had a sharp disagreeable empyreumatic odour. The distillate from this fluid reduced nitrate of silver (formic acid?). Nothing was extracted by æther from the residual fluid, which had an acid reaction, and formed, with barium, an insoluble crystalline precipitate of unknown composition.

In the decomposition of cerebrine by sulphuric acid, its nitrogen appears to be partly at least given off as free ammonia, as I obtained a precipitate of ammonium-platinum-chloride, on adding chloride of platinum to the sulphuric solution.

I have determined the acid nature of the copper-reducing substance, which is produced at the same time and dissolves in water. It forms salts which resist the action of carbonic acid. It appears to deflect polarised light to the left, in the same manner as the substances which are obtained from mucine, chondrine, and the urine of animals poisoned with chloral and carbonic oxide. I have failed as yet to obtain it pure.

This last acid appears in many ways to resemble Uramidocamphoglycuronic acid, described by Schmiedeberg and Meyer* in the last number of "Hoppe Seyler's Journal."

On the Connection between the Mental State and Inequality of the Pupils in General Paralysis. By FRANCIS WYATT THURNAM, M.B., Assistant Medical Officer, Bristol Borough Asylum.

Out of 946 cases admitted into the Bristol Asylum since January, 1870, symptoms of General Paralysis of the Insane have existed in 116; of which 83 occurred in males, and 33 in females, the admissions being respectively 440 males and 506 females.

The percentages thus are—

18·863	amongst	Insane	Males.
6·521	„	„	Females.
12·162	„	„	of both Sexes.

* O. Schmiedeberg and H. Meyer, Ueber Stoffwechselprodukte nach Campher fütterung, "Zeitschrift für physiol. Chemie." III., 6, p. 451, Nov. 7, 1879.