

III. "Researches conducted for the Medical Department of the Privy Council at the Pathological Laboratory of St. Thomas's Hospital." By J. L. W. THUDICHUM, M.D. Communicated by JOHN SIMON, Esq., Medical Officer of the Privy Council. First Series.—The Chemical Nature and Composition, Combinations, and Metamorphoses of the Colouring-matters of Bile. Received November 14, 1867.

(Abstract.)

I. On *Cholophæine* or *Bilirubine* and its Compounds.

Sect. 1. The paper commences with a short historical retrospect on the literature of the subject under consideration, in which the researches of Berzelius, Scherer, Hein, Marchand, Heintz, Maly, and Städeler are mentioned. Sect. 2. The author then describes the mode of obtaining a red colouring-matter from ox-gallstones. These concretions have to be extracted with water, alcohol, ether, dilute hydrochloric acid, and ultimately, after repeated extraction with boiling alcohol and ether, with chloroform. This agent dissolves *bilirubine* or *cholophæine*, and deposits it, on concentration and the addition of absolute alcohol, in an amorphous condition, or in a crystallized state. Sect. 3. The crystals are dark brown, and have a splendid blue lustre. They are rhombic plates, as represented by a drawing in outline taken from a specimen magnified about twenty times. The amorphous or only crystalline modification is a powder of a splendid red, nearly orange-colour. Sect. 4. The elementary analysis of several specimens yielded results which led to the formula $C_9 H_9 N O_2$. Sect. 5. *Bilirubine* dissolves in ammonia, but does not form any permanent compound with it. Its combinations with fixed caustic alkalies are insoluble in an excess of lye. The neutral alkali solution, mostly the one in ammonia, yields neutral salts with monodynamic metals, half-acid salts with didynamic ones.

The *neutral monohydrated cholophæinate of silver*, $C_9 H_{10} Ag NO_3$, $Ag=37.5$ per cent., is a reddish-brown precipitate, which does not lose the atom of water at $110^\circ C$. As a hydrated silver-salt it is anomalous; but a few other animal products, such as hippuric acid, are known also to form such hydrated silver-salts. By means of this compound, the formula of *bilirubine*, or *cholophæine*, above given, is shown to express its atomic weight.

The *basic anhydrous cholophæinate of silver*, $C_9 H_7 Ag_2 NO_2$, $Ag=57.29$ per cent., is obtained from an alkaline solution of *cholophæine* and silver nitrate in ammonia, by cautiously reducing the amount of free alkali by means of nitric acid. The compound is analogous to a lead-salt, $C_9 H_7 Pb NO_2$ described lower down.

The *neutral cholophæinate of barium* is precipitated from an alkaline solution, and has the composition $C_{18} H_{20} Ba N_2 O_6$, $Ba=27.56$ per cent.

The *half-acid cholophæinate* or *sesquicholophæinate* is $C_{27} H_{29} Ba$

$\text{N}_3 \text{O}_8$, Ba = 20·75 per cent., and precipitated by neutral Ba salts from a neutral solution in ammonia. The differences between these salts were established in all their details by analyses, the means of which compare with theory as follows:—

	Neutral salt. Atom. W. 477.		Half-acid salt. Atom. W. 660.	
	Theory.	Found.	Theory.	Found.
C	43·46	44·58	49·09	50·63
H	4·02	3·98	4·39	4·37
Ba	27·56	27·55	20·75	20·66

The discovery of these salts was of particular importance, as they led to the discovery of similar calcium compounds, and thereby to important theoretical developments.

	The neutral calcium-salt, $\text{C}_{18} \text{H}_{20} \text{Ca} \text{N}_2 \text{O}_6$. Atom. W. 400.		The half-acid calcium-salt, $\text{C}_{27} \text{H}_{28} \text{Ca} \text{N}_3 \text{O}_8$. Atom. W. 563.	
	Theory.	Found.	Theory.	Found.
C	54	53·86	57·54	60·37
H	5	4·90	5·15	5·74
Ca	10	10·17	7·10	6·91

The calcium compound, on the basis of which Städelér had assumed $\text{C}_{18} \text{H}_{18} \text{N}_2 \text{O}_3$ to be the atomic formula of bilirubine, had yielded him (one analysis) 9·1 per cent. of calcium oxide, therefore less calcium than was found in the analysis of the half-acid salt, or 6·5 per cent. There is no doubt that Städelér had this half-acid compound before him. He unfortunately obtained the most unstable and uncertain of all the compounds of bilirubine, and mistook it for a neutral salt, abandoning his former correct analysis and formula of free bilirubine. With Städelér's last formula of bilirubine fall the formulæ of all other substances described by him under the names of biliverdine, biliprasin, bilifuscine, and bilihumine.

The *half-acid cholophæinate of zinc*, $\text{C}_{27} \text{H}_{28} \text{Zn} \text{N}_3 \text{O}_8$, with 11·05 per cent. of Zn , and the *neutral cholophæinate of lead*, $\text{C}_{18} \text{H}_{20} \text{Pb} \text{N}_2 \text{O}_6$, Pb = 36·50 per cent., were also obtained. *Basic cholophæinate of lead* is analogous to the basic silver-salt, as in it two atoms of hydrogen are replaced by one didynamic atom of lead. Formula = $\text{C}_9 \text{H}_7 \text{Pb} \text{NO}_2$, Pb = 56·25 per cent.

Some *copper compounds* were also obtained.

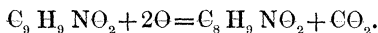
A new reaction for cholophæine is given. It consists in dissolving the dry powder in fuming sulphuric acid. A splendid green is at once produced. The substance is not biliverdine, but a product which, when isolated, contains an atom of water more than bilirubine, and is $\text{C}_9 \text{H}_{11} \text{NO}_3$, and is named cholothalline by the author. Cholothalline colours wool of a fast green, indestructible by acid, discharged by ammonia.

Cholophæine also yields a blue-coloured substance by treatment with

nitric acid (cholocyanine), of which the peculiar spectrum was determined. A great number of green, blue, violet, and red bodies can be produced by appropriate agents, which, if they could be obtained on a large scale, might find technical application.

II. On Biliverdine or Cholochlorine and its Compounds.

Sect. 1 treats of the mode of obtaining biliverdine. Cholphæine is dissolved in carbonate of potassium, and warmed while a current of air is passed through it. When the solution is green, it is precipitated with hydrochloric acid. The precipitated biliverdine is easily soluble in alcohol. Sect. 2 describes the physical properties of biliverdine, as a non-crystalline splendidly green substance, the solution of which gives no particular absorption phenomena in the spectrum. Sect 3 gives the elementary analyses and theory of biliverdine, which led to the formula $C_8 H_9 NO_2$. Thus it was shown that it originated from cholophæine by the addition of oxygen and subsequent subtraction of carbonic acid.



Sect. 4. treats of the compounds of biliverdine. The calcium-salt was not obtained pure. The barium-salt appeared to be $C_{24} H_{27} Ba N_3 O_7$, and was precipitated by baryta-water from an alcoholic solution of biliverdine. It consequently consisted of one atom of the neutral salt with an atom of biliverdine and one of water. Lead and copper compounds were also obtained. No insoluble silver-salt could be obtained. The addition of oxide of silver to an alcoholic solution caused a reaction, consisting in an oxidation of the biliverdine.

A new reaction for biliverdine is stated. When dissolved in alcoholic ammonia, and boiled with an ammoniacal solution of silver nitrate, silver is deposited, and on addition of an acid a splendid purple matter is produced (bilipurpine).

Of these new substances and others the author hopes to treat in future communications.

Chlorine and other substitution-products are also mentioned.

The foregoing contributions will make the chemistry of the bile in the main complete. Human bile contains cholophæine, but most commonly by the side of it *bilifuscine*, a brown substance to be treated of hereafter.

Second Series.—The Chemical Nature and Composition, Combinations and Metamorphoses of the Colouring-matter of the Urine.

I. On Uromelanine, a product of decomposition of Urochrome.

In the Hastings Prize Essay for 1864 the author described a substance to which he gave the name of Uromelanine, on account of its origin and black colour. He now describes the method of obtaining it from putrid urine as well as fresh, and a method of purification by which it is obtained of uniform composition and in a pseudo-crystalline condition.

He has prepared twelve specimens by various processes, and analyzed many of them, as well as a great number of their compounds, with various metals. These preparations are marked respectively as in the following list :—

Prize Essay preparations. Compounds.

By boiling with H_2SO_4 :—

A. I. From fresh urine. Elementary analyses. Neutral. Ba salt ($\tilde{U}r_2Ba$), Zn salt ($\tilde{U}r_3Zn_2$), Pb salt ($\tilde{U}r_3Pb_2$).

A. II. From fresh urine. Ag salt ($\tilde{U}rAg$), Ba salt ($\tilde{U}r_4Ba_3$).

By addition of H_2SO_4 , no boiling :—

A. III. From putrid urine. Ag salt ($\tilde{U}rAg$), Ba salt ($\tilde{U}r_4Ba_3$), Ca salt ($\tilde{U}r_4Ca_3$).

Preparations made for the present research.

By boiling with H_2SO_4 :—

B. I.

B. II. Two elementary analyses.

B. III.

Before boiling with H_2SO_4 :—

C. I.

After boiling :—

C. II. Six elementary analyses.

Before boiling :—

D. I. Two N determinations. $N=13.58$ per cent. Ag salt ($\tilde{U}r_2Ag_3$), Ca salt ($\tilde{U}r_3Ca$) and ($\tilde{U}r_2Ca_3$), Zinc-salt ($\tilde{U}r_3Zn$).

After boiling with H_2SO_4 :—

D. II.

D. III.

D. IV. Two N determinations. $N=12.40$ per cent. Ag salt ($\tilde{U}r_3Ag_3$), Ba salt ($\tilde{U}r_2Ba$) and Zinc-salt ($\tilde{U}r_3Zn$).

Synopsis of Uromelanates obtained with the foregoing preparations.

Silver-salts.

Preparation.	$\tilde{U}r \div Ag$.	Ag. found.
(A. II.), (A. III.) .	$1 \div 1$	13.38 per cent.
(D. I.)	$2 \div 3$	18.57 „
(D. IV.)	$3 \div 5$	19.77 „

Barium-salts.

	$\tilde{U}r \div Ba$.	Ba found.
(D. IV.)	$5 \div 2$	7.20 per cent.
(A. I.), (D. IV.) .	$2 \div 1$	8.34 „
(A. II.), (A. III.) .	$4 \div 3$	13.28 „

Calcium-salts.

	$\tilde{\text{Ur}} \div \text{Ca.}$	Ca found.
(D. I.)	$5 \div 2$	2.03 per cent.
(A. II.)	$4 \div 3$	4.35 „
(D. I.)	$2 \div 3$	7.27 „

Zinc-salts.

	$\tilde{\text{Ur}} \div \text{Zn.}$	Zn found.
(D. I.)	$3 \div 1$	2.82 per cent.
(A. I.)	$5 \div 2$	3.54 „
(D. IV.)	$2 \div 1$	4.42 „

Lead-salt.

	$\tilde{\text{Ur}} \div \text{Pb.}$	Pb found.
(A. I.)	$3 \div 2$	15.70 per cent.

The analyses of (A. I.), (A. III.), (D. I.), (D. IV.), and of the two-thirds basic silver-salt ($\tilde{\text{Ur}}_3 \text{Ag}_5$) determined uromelanine to be $\text{C}_{36} \text{H}_4 \text{N}_7 \text{O}_{10}$.

	Theory of atoms.	Per cent.	Found, mean.
C_{36}	432	58.93	57.21
H_{43}	43	5.86	5.74
N_7	98	13.36	12.88
O_{10}	160	21.85	24.17
	<u>733</u>	<u>100.00</u>	<u>100.00</u>

The *normal silver-salt* is $\text{C}_{36} \text{H}_{40} \text{Ag} \text{N}_7 \text{O}_9$, and is therefore $\tilde{\text{Ur}} + \text{Ag} - \text{H}_3 \text{O}$. One atom of water leaves $\tilde{\text{Ur}}$ when Ag enters, besides H.

The *half-basic silver-salt* shows no loss of water.

The *two-thirds basic silver-salt*, $\tilde{\text{Ur}}_3 \text{Ag}_5$, is an exceedingly well-defined compound. Its formula is $\text{C}_{108} \text{H}_{124} \text{Ag}_5 \text{N}_{21} \text{O}_{30}$.

	Required in 100.	Found.
C	47.40	46.90
H	4.53	4.77
Ag	19.75	19.77
N	10.75	10.36
O	17.57	18.20
	<u>100.00</u>	<u>100.00</u>

The other nine salts mentioned in the synopsis have all been analyzed. They support each other's theory, and the details of their description must be seen in the main paper.

Uromelanine is a product of decomposition of the yellow-coloured ingredient of the urine, urochrome. Its atomic weight (733) is higher than that of any other product of decomposition of animal or organic matter; it contains neither sulphur nor iron. While the analyses of

cholophæine and biliverdine have shown that they have no apparent relation to hematine, as was formerly supposed, the analyses of uromelanine have made it probable that this substance is a derivative of the coloured part of the blood, cruorine or hematocrystalline, not, however, of hematine, for the atomic weight of hematine is apparently smaller than that of uromelanine. But crystallized cruorine has an atomic weight of about 13,000 ($\text{Fe} = 0.45$ per cent.). From such a body urochrome, including as it does uromelanine, uropittine, omicholine, and perhaps other matters (to be described in future communications), might be derived with an atomic weight of perhaps 1500, being itself near that of albumen (1612), but unable to derive from it. The author thinks it possible that the quantity of blood-disintegration might be measured by determining the amount of uromelanine obtainable from given quantities of urine excreted in given times. In any case uromelanine is one of the most remarkable substances in the whole domain of organic and animal chemistry, and the further study of its metamorphoses cannot fail to yield highly interesting results.

December 19, 1867.

Lieut.-General SABINE, President, in the Chair.

Pursuant to notice given at the last Meeting, Professor Stokes proposed, and Mr. De la Rue seconded, the Right Honourable the Earl of Rosse for election and immediate ballot.

The ballot having been taken, the Earl of Rosse was declared duly elected.

The Bakerian Lecture, "Researches on Vanadium," was delivered by Prof. H. E. Roscoe, Ph.D., F.R.S.

THE BAKERIAN LECTURE.—"Researches on Vanadium."—Part I. By HENRY E. ROSCOE, B.A., F.R.S. Received November 20, 1867.

(Abstract.)

I. *Introduction.*

Amongst the physical properties which point out the general relationship and classification of chemical compounds, none has so deservedly obtained the confidence of chemists as isomorphism. The vanadium compounds have, however, proved a remarkable and unexplained exception to the conclusions which generally follow from well ascertained identity of crystalline form. Rammelsberg, and afterwards, more completely, Schabus, pointed out the fact that the mineral vanadinite from several localities (a compound of lead vanadate and lead chloride) is isomorphous with apatite, pyromorphite, and mimetosite, minerals consisting of calcium phosphato-chloride, lead phosphato-chloride, and lead arsenato-chloride.

The crystalline form of all these minerals is an hexagonal prism, terminated by 6-sided pyramids. So far indeed has the isomorphism of these