VI.—*On Quinicine and Cinchonicine and their Salts.*

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IN the early part of last year I brought before the notice of this Society an account of an alkaloid from cinchona bark, the properties of which distinguished it from those already described.

Further investigations, following out a suggestion which I owe to

Dr. de Vrij, of the Hague, convince me that it is identical with the quinicine, first obtained by Pasteur from quinine by the action of heat, and described by him in a paper, a translation of which is to be found in the Journal of the Chemical Society, vol. vi, p. 274.

I now supplement the brief account there given by a more particular description of the crystalline salts of this singular alkaloid, and of the similarly formed cinchonine, the allusions to which are very slight in Pasteur's paper; and believe that the result of a further examination will be found to add something to our knowledge of the history of the cinchona alkaloids, and to throw some light on the vexed question of the identity of quinicine with the uncrystallised alkaloids contained in these barks, which in an impure state form the quinoidine of commerce, which Pasteur suggests in the above-mentioned paper, but which still remains undecided.

The result of many experiments on the transformation of quinine and quinidine into quinicine; and of cinchonine and cinchonidine into cinchonine, confirm Pasteur's observations that, "though heat plays an important part in this transformation, the vitreous resinoidal state of the product has nevertheless a real influence on it." Thus we find that the action of heat on a solution of a salt of an alkaloid in water in sealed tubes, even when exposed to a higher temperature than is required under favourable circumstances to convert it wholly into the isomeric modification, is very slight indeed; if, however, a considerable excess of acid be present, the alkaloid is, under the same circumstances, slowly changed, but far less readily than when Pasteur's conditions are observed. On the other hand, acting on a hint of Dr. de Vrij's, I find that a mixture of glycerin and neutral sulphate of cinchonine, exposed to the needful heat, is converted into sulphate of cinchonine *pari passu* with a mixture of the salt with acid. Sulphate of quinine when heated with glycerin, showed no signs of the formation of quinicine, owing apparently to the slight solubility of the salt in that medium.

The change in the alkaloids is accompanied in all cases by the development of a yellow colour, which seems inherent in the resulting alkaloid; if more heat is used than is absolutely needed, especially when atmospheric air is present, a further decomposition takes place with formation of a darker colour; this may be in great part prevented by heating in an atmosphere of carbonic anhydride.

A careful examination of the salts of quinicine shows that the alkaloid described in my previous paper is identical with it. The greater number of these salts are difficult to crystallise, but the chloroplatinate, the oxalate, and the acid tartrate crystallise with comparative ease, and can be obtained in a state of purity. We are thus enabled to observe a fact of some importance, that the salts of quinicine pre-

pared from quinine are exactly similar in all their properties to those prepared from quinidine; in fact, that there is but one quinicine, from whichever of the isomeric bases it may have been derived.

The chloroplatinate precipitated from a hot solution forms a crystalline powder; it can be obtained in definite crystals from a hot acid solution. Its formula is $C_{20}H_{24}N_2O_2 \cdot 2HCl.PtCl_4$. Analysis gives the following results:—

	Pt.
Chloroplatinate of alkaloid prepared from quinine ..	26·58 p. c.
” ” ” ” ” ..	26·42
” ” ” ” quinidine..	26·45
” ” ” ” extracted from quinoidine	26·63
Theory requires	26·76

The oxalate, as previously described, has the formula, $2C_{20}H_{24}N_2O_2 \cdot C_2H_2O_4 + 9H_2O$. The analysis gives results as under—

	$C_2H_2O_4$.	H_2O . 7 at. lost <i>in vacuo</i> .	H_2O . 9 at. lost at 100 c.
Theory	10·00	14·00	18·00
Average of previous determinations of oxalate from quinoidine	10·11	14·04	17·91
Oxalate of quinicine prepared from quinine	9·99	14·37	18·02
Oxalate of quinicine prepared from quinidine	—	13·90	18·05
Oxalate of quinicine prepared from quinidine	9·96	14·08	17·83
	—	14·00	17·83

The acid tartrate crystallises freely from strong solutions in radiated needles; the determinations of H_2O and $C_4H_6O_6$ agree with the formula, $C_{20}H_{24}N_2O_2 \cdot C_4H_6O_6 + 6H_2O$. The salt fuses readily when exposed to a heat of $100^\circ C$. By gradual drying at about 50° , it loses 4 atoms of water; and by heating to 140° , the remaining 2 atoms are expelled, with fusion of the salt and slight discoloration. Analysis gives the following figures:—

	$C_4H_6O_6$.	H_2O . 4 at. lost at 50 c.	H_2O . 6 at. lost at 140 c.
Theory	25·77	12·37	18·56
Acid tartrate of quinicine prepared } I. from quinine	26·05	12·80	19·36
Acid tartrate of quinicine prepared } II. from quinine	25·29	13·00	—
Acid tartrate of quinicine prepared } I. from quinidine	25·26	11·97	19·31
Acid tartrate of quinicine prepared } II. from quinidine	25·23	11·83	18·88
Acid tartrate of quinicine prepared } I. from quinoidine	25·97	13·55	17·99
Acid tartrate of quinicine prepared } II. from quinoidine	25·66	13·00	19·29

Cinchonidine and its salts are very similar in their properties to quinicine and its salts; the alkaloid is soluble in ether, separating

like quinine, as an oily layer at the bottom of the solution as the ether evaporates. The salts are somewhat more soluble than the corresponding quinine salts. The same identity is observed between those prepared from cinchonine and those from cinchonidine that is found between the salts of quinine prepared from quinine and from quinidine.

The *platinochloride* gives the following results, showing the formula to be $C_{20}H_{24}N_2O \cdot 2HCl \cdot PtCl_4$:—

	Pt.
Theory	27·36
Platinochloride of cinchonicine prepared from } cinchonine	27·65 27·61
Platinochloride of cinchonicine prepared from } cinchonidine	27·52 27·63

The *oxalate* differs from the oxalate of quinine by containing only 7 atoms of water ; it very readily loses a portion of this water, and is therefore difficult to dry for analysis ; the whole is given off at $100^\circ C$. No definite point of hydration is reached by drying *in vacuo*. It is somewhat more soluble than the quinine salt.

Analysis gives the following results :—

$2C_{20}H_{24}N_2O \cdot C_2H_2O_4 + 7H_2O$ require—

	$C_2H_2O_4$ 10·82.	$7H_2O$ 15·14.
Oxalate of cinchonicine prepared from } cinchonine gives	11·06 10·90 11·07	14·30 15·18 —
Oxalate of cinchonicine prepared from } cinchonidine	11·00 11·05	14·76 15·55

The *acid tartrate* crystallises in crusts composed of short prisms ; this salt contains but one atom of water, which it loses at $120^\circ C$. without fusion.

The formula, $C_{20}H_{24}N_2O \cdot C_4H_6O_6 + H_2O$ requires—

	$C_4H_6O_6$ 31·51.	H_2O 3·70.
Acid tartrate of cinchonicine prepared from } cinchonine gives	32·49 31·33	3·83 3·80
Acid tartrate of cinchonicine prepared from } cinchonidine	32·27	3·68

The action of these alkaloids on polarised light also shows the

identity of the resulting alkaloid produced by the action of heat on the isomeric alkaloids, the different action on the polarised ray disappearing with the other characteristic distinctions. Quinicine, either from the strongly levogyrate quinine, or from the dextrogyrate quinidine, exhibits a comparatively feeble right-handed rotation, identical within the limits of errors of observation.

The observed molecular rotatory powers of these alkaloids for the yellow ray are as follows :—

In a spiritous solution of the alkaloid—

Quinicine from quinine	 $\nearrow 39^\circ$
Quinicine from quinidine	 $\nearrow 39^\circ$
Quinicine from quinoïdine	 $\nearrow 39.3^\circ$

Oxalate of quinicine in an acid solution—

Prepared from quinine	 $\nearrow 13.4^\circ$
Prepared from quinidine	 $\nearrow 14^\circ$
Prepared from quinoïdine	 $\nearrow 14^\circ$

Cinchonidine in a spiritous solution—

Prepared from cinchonine	 $\nearrow 48^\circ$
Prepared from cinchonidine	.. $\nearrow 48.4^\circ$

Oxalate of cinchonidine in an acid solution—

From cinchonine	 $\nearrow 18^\circ$
From cinchonidine	 $\nearrow 17.9^\circ$

It will be observed that the rotatory power in both cases is much less in an acid solution than in a spiritous solution of the alkaloid.

It is very difficult to determine what is the exact nature of the change we have been considering. The examination of the optical and chemical properties of successive crystallisations of these salts fails to detect signs of the existence of more than one homogeneous product. The high colour of some of the later crystallisations prevented the use of solutions in the polarimeter strong enough to give more than a very small angle of rotation, and perfectly accordant results are thus unattainable. Still the differences observed between the first and the last crystallisations from considerable quantities are too small to throw doubt on their identity.

Thus the molecular rotation observed in the oxalate of quinicine from the mother-liquor of salts of the alkaloid prepared from quinine was $\nearrow 13.3^\circ$, and of the alkaloid in solution in spirit $\nearrow 31.6^\circ$; that of similarly prepared oxalate from quinidine $\nearrow 12.2^\circ$. Cinchonidine from the last mother-liquors prepared from cinchonine showed a rotatory power of $\nearrow 44.5^\circ$, and its oxalate $\nearrow 18.5^\circ$, while the last portions prepared from cinchonidine showed $\nearrow 40^\circ$.

The question now arises: is the uncrystallisable alkaloid obtained from chinchona bark quinine, or is it yet another alkaloid really uncrystallisable. Hitherto the most careful purification has failed to obtain crystalline salts from it such as have been described. When quinine is present, it will, as has been stated, crystallise out of the mixture, but the bulk of the quinoïdine, however carefully purified, refuses to crystallise even after many months' standing. It seems highly improbable, though of course it is possible, that this is owing to some impurity which hinders the crystallisation: for we find that quinine-salts prepared from crystallisable alkaloid crystallise entirely with comparative freedom, even when the heat used in its formation has been considerably above the point needed, and sufficient to decompose a portion, and there is no sign of any amorphous modification being formed.

Quinoïdine closely resembles quinine in other respects. When purified, as far as possible, by fractional precipitation and solution in ether, it forms a readily fusible yellow resin. The platinochloride precipitates as an amorphous powder, readily fusible, slightly soluble in hot water, and much more so in hot dilute hydrochloric acid, from its solution in which it falls out on cooling, as an amorphous powder, which under the microscope appears to consist of globules without any sign of crystallisation.

The salt precipitated from a cold solution contains 26.59 per cent. of platinum, and after solution in dilute acid 26.28 per cent.; it is, therefore, isomeric with quinine and quinine.

It is difficult to speak with certainty of the optical properties of this alkaloid, on account of the great difficulty of insuring absolute purity from the other alkaloids of higher rotatory power, a very small percentage of which would evidently vitiate the results. The specimen, the analysis of the platinum salt of which is given above, showed a specific rotatory power of $\alpha_{D}^{20} 33^{\circ}$; other specimens gave higher results, but their purity was more doubtful.