The physiological action of quinoline, isoquinoline and some of there derivatives / by Ralph Stockman.

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THE PHYSIOLOGICAL ACTION OF QUINOLINE, ISOQUINOLINE AND SOME OF THEIR DERIVATIVES.

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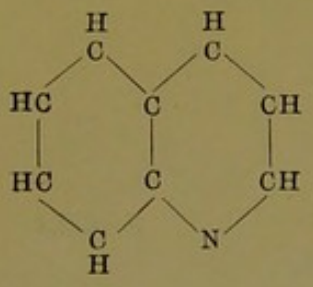
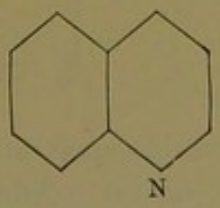
In quinoline, isoquinoline, and certain of their immediate derivatives, one has a number of isomeric alkaloids of nearly similar constitution, but having certain of their atoms or radicals differently placed in relation to each other. It occurred to me that it would be of interest to ascertain whether those slight differences in chemical constitution exert any appreciable influence on the physiological action of the bodies in question, more especially as a number of complex alkaloids (such as quinine, cinchonine, strychnine, morphine) are thought to be derived from quinoline, while recently it has been proved that others (such as berberine, narcotine, papaverine and hydrastine) are derived from isoquinoline.

Quinoline (C_9H_7N) has the following constitution:



but for convenience it is often expressed thus;



it being understood that CH or C are attached at the unoccupied points of the rings.

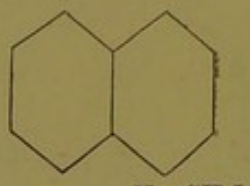
Isoquinoline is isomeric with it, the only difference being that the atom of nitrogen occupies a different position.

The action of quinoline has often been investigated. It is a strong antiseptic and antipyretic, and depresses the central nervous system. I made comparative experiments with it and with isoquinoline on frogs and rabbits, and found that there was no appreciable difference in the action of the two bodies. That is to say, 2½ milligrams of the tartrate of either alkaloid was sufficient to cause marked depression of the spinal cord in frogs, the animals recovering after some hours. Larger doses depressed both brain and cord, this being succeeded by very slight exaggeration of reflexes. The heart and motor nerves are only affected by very large doses.

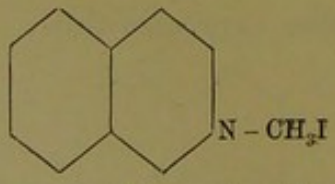
In rabbits about 3 decigrams of either tartrate given subcutaneously slowed the respiration somewhat and produced usually a trifling fall of temperature; but 1 to 1½ grams caused more or less collapse, marked depression of the nervous system, and a very great fall of temperature. The respiration was greatly slowed, and the heart markedly so.

I could detect no difference, either qualitative or quantitative, in the actions of the two substances.

Quinoline methiodide



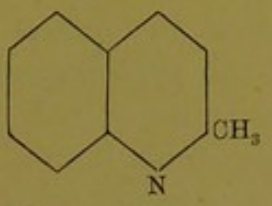
and isoquinoline methiodide



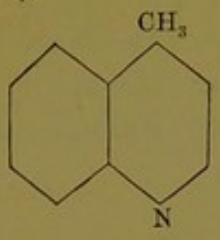
were also found to exactly resemble each other in physiological action. They are made by simply adding on iodide of methyl to the original molecule, and like all such addition products they retain essentially the same action as the alkaloids from which they are derived, but have a

much more paralysing action on the terminations of motor nerves[1]. In frogs 5 milligrams cause marked depression of the spinal cord followed by increased reflexes, larger doses have a more or less marked paralysing action on the terminations of motor nerves and this masks the other symptoms somewhat. In rabbits 3—5 decigrams cause death from paralysis of motor nerves, but there is considerable general collapse and fall of temperature.

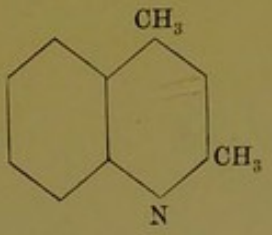
I have also examined the physiological action of *quinaldine* (*a*-methylquinoline),



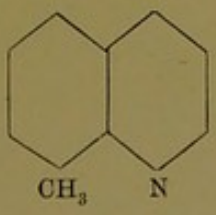
of lepidine (γ-methylquinoline),



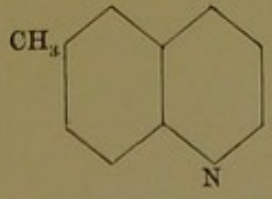
of *a*-γ-dimethylquinoline,



of orthotoluquinoline,



and of paratoluquinoline,



[1] Stockman and Dott. *Proc. Roy. Soc. Edin.* 1889–90, and *Brit. Med. Journ.* I. 1891.

Tartrate of quinaldine has, on frogs and rabbits, an action similar to that of quinoline or isoquinoline, but it is somewhat less active. The dimethylquinoline is still less active, and therefore it would appear that the substitution of methyl radicals for hydrogen atoms in quinoline weakens its depressing action on the nervous system.

With the other substances observations were made on frogs only, the sulphates, which are fine white crystalline salts, being used. Their actions seemed similar in every respect to that of quinaldine.

It is evident, therefore, that in the quinoline molecule, the position of the nitrogen atom, or of the radical methyl does not exert any appreciable influence on the physiological action of these substances, and further that the substitution of CH_3 for H only slightly alters its action, and that only in degree not in kind. It is improbable also that the derivation of a more complex alkaloid from quinoline or isoquinoline respectively is in any way a factor which determines its action, seeing that these two substances have exactly similar actions. All the substances used were chemically pure. Some of them were kindly given me by Professor Perkin, of Manchester, some I made myself, others were bought.