

THE CAUSE OF IRRITATION OF 8-HYDROXY QUINOLINE COMPOUNDS. ONE EFFECT OF p_H CAUSED BY ACID MOLECULE.*

BY R. VAN WINKLE AND W. G. CHRISTIANSEN.

8-Hydroxy quinoline compounds have been shown to exert a strong antiseptic action. Their use as an antiseptic, has been restricted due to the accompanying irritation to the mucous membrane which they cause. The latter is not uniformly noticed inasmuch as some individuals are highly susceptible to this irritation while others are almost entirely immune to it. The following work was carried out in order to determine whether the acid molecule attached to the 8-hydroxy quinoline nucleus bore any relation to the above-mentioned irritation.

PREPARATIONS.

8-Hydroxy Quinoline Sulphate.—5.8 Gm. of dry 8-hydroxy quinoline were dissolved in 10 cc. of tertiary butyl alcohol and 2.12 Gm. of concentrated sulphuric acid were dissolved in 10 cc. of 95% ethyl alcohol. The acid was added slowly to the base with stirring and a yellow precipitate was obtained immediately. The latter was filtered off, washed with alcohol and dried at 55° C.

	Melting point	176°–179° C.
Analysis	Found	6.78%, 6.85% nitrogen
	Calculated $(C_9H_7ON)_2 \cdot H_2SO_4 \cdot H_2O$	6.89% nitrogen

The above material is sold commercially as "Chinosol" and the latter material analyses 6.88%, 6.85% nitrogen.

Solubility—70.5 Gm./100 cc. of saturated solution.

8-Hydroxy Quinoline Salicylate.—5.8 Gm. of 8-hydroxy quinoline were dissolved in 20 cc. of tertiary butyl alcohol and 5.52 Gm. of dry salicylic acid were dissolved in 10 cc. of 95% ethyl alcohol. The acid was added slowly to the base with stirring. The yellow compound obtained was filtered off, washed and dried at 55° C.

	Melting point	114°–116° C.
Analysis	Found	4.99%, 5.09% nitrogen
	Calculated $(C_9H_7ON) \cdot (C_7H_6O_2)$	4.95% nitrogen

Solubility—0.59 Gm./100 cc. of saturated solution.

8-Hydroxy Quinoline β -Resorcylate.—5.8 Gm. of 8-hydroxy quinoline were dissolved in 10 cc. of tertiary butyl alcohol and 8.52 Gm. of β -resorcyclic acid were dissolved in 20 cc. of 95% ethyl alcohol. The acid was added slowly to the base and the yellow compound obtained was washed and dried at 55° C.

	Melting point	154°–156° C.
Analysis	Found	4.61% nitrogen
	Calculated $(C_9H_7ON) \cdot (C_7H_6O_4)$	4.68% nitrogen

Solubility—0.53 Gm./100 cc. of saturated solution.

8-Hydroxy Quinoline Tartrate.—2.9 Gm. of 8-hydroxy quinoline were dissolved in 8 cc. of tertiary butyl alcohol and 3 Gm. of dry tartaric acid were dissolved in 15 cc. of 95% ethyl alcohol. The base was added slowly to the acid. The

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	Inhibited.				Typhoid.			
	Staphylococcus.							
8-Hydroxy quinoline β -resorcyate								
1- 50,000	—	—	—	x	—	—	—	x
1-100,000	—	—	x	x	—	—	x	x
1-150,000	—	—	x	x	—	—	x	x
1-200,000	x	x	x	x	x	x	x	x
8-Hydroxy quinoline salicylate								
1- 50,000	—	—	x	x	—	—	x	x
1-100,000	—	—	x	x	—	—	x	x
1-150,000	—	—	x	x	—	—	x	x
1-200,000	x	x	x	x	x	x	x	x
8-Hydroxy quinoline tartrate								
1- 50,000	—	—	x	x	—	—	x	x
1-100,000	—	—	x	x	—	—	x	x
1-150,000	—	x	x	x	—	x	x	x
1-200,000	x	x	x	x	x	x	x	x

IRRITATION TESTS.

This test was carried out by putting a drop of a 1-1000 solution in the eye of five individuals. At least twenty-four hours elapsed between tests on each individual.

	Strong irritation.	Slight irritation.	Irritation.
8-Hydroxy quinoline β -resorcyate		2	3
8-Hydroxy quinoline tartrate		3	2
8-Hydroxy quinoline citrate		4	1
8-Hydroxy quinoline salicylate	1	4	
8-Hydroxy quinoline sulphate	1	4	

Distilled Water—Solvent—two observed a slight sting but it was highly different from the irritation of the above solutions.

CONCLUSIONS.

From our data it is indicated that

1. Changing of the acid molecule of 8-hydroxy quinoline compounds has very little effect on the antiseptic action of the latter. The sulphate, citrate and β -resorcyate are the best and equally efficient. They inhibit the growth of Staphylococcus and Typhoid bacteria at a dilution of 1-50,000 for seventy-two hours.

2. Changing of the acid molecule affects the germicidal activity of 8-hydroxy quinoline to some extent. The sulphate and citrate were shown to be the most efficient in this respect. A 1-2000 solution of either killed staphylococcus in one minute.

3. No definite relation was found to exist between irritation and the p_H variation caused by the different acid molecules attached to the quinoline nucleus. The two extreme compounds, sulphate and β -resorcyate would tend to indicate some such relation but the intermediate ones do not substantiate such a conclusion. We are led to believe accordingly that the irritation is in all probability a factor of the 8-hydroxy quinoline nucleus itself rather than a factor of the p_H of the aqueous solution caused by the acid molecule attached to it.

RESEARCH DEPARTMENT OF THE CHEMICAL
AND PHARMACEUTICAL LABORATORIES,
E. R. SQUIBB & SONS, BROOKLYN, N. Y.