

rate of involution of wheals of pollen or histamine was little influenced by epinephrine when compared with the control rate for that individual but itching was often much less after epinephrin. This drug in the above amount did not prevent the formation of definite positive skin reactions, in fact a few patients gave as large or larger reactions after epinephrin as before. In the majority the reaction for one dilution was similar to that produced by the next higher dilution before the injection of epinephrin, thus the drug decreased the reaction about as much as would result from a 1-10 dilution of the test substance. The secondary erythema was markedly decreased by the drug in most cases.

A few tests have been made with twice the dose of epinephrin indicated above. By the use of the larger dose more marked interference with the genesis of a positive wheal was evident.

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The Effect of Alkalis Upon the Solubility of Quinine Salts.

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The present study was suggested by the paper by Eggleston¹ pointing out the need for further experimental data concerning factors influencing the absorption of drugs from the gastro-intestinal tract. The literature reveals a surprising dearth of material, particularly as relating to the rôle of hydrogen ion concentration as a factor in absorption.

The immediate problem was the determination of the solubility of soluble quinine salts (hydrochloride, dihydrochloride and bisulphate) in solutions of various alkaline salts at various concentrations and pH, when equal parts of 2% quinine salt and alkaline salt were mixed. The alkaline salts employed were K_2HPO_4 , Na acetate, Na citrate, $NaHCO_3$ and Na_2CO_3 . The effect of OH ion was learned through the use of NaOH. An end concentration of 1% quinine salt was thought to approximate the expected concentration in the stomach and duodenum after a full therapeutic dose of quinine. The pH determinations were made colorimetrically, using the

¹ Eggleston, C., *J. Am. Med. Assn.*, 1923, lxxxi, 431.

Michaelis² one-color series without buffers, and these values checked by the quinhydrone electrode.

TABLE I
Percentage of Alkali Used and Beginning Precipitation Points with pH Values.

Alkali	Quinine-HCl		Quinine-Di-HCl		Quinine-Bi-SO ₄	
	pH	%	pH	%	pH	%
Potassium Basic Phosphate	7.07	.05	3.45	.7	3.64	.2
Sodium Hydroxide	7.12	N/300	3.40	N/10	2.89	N/150
Sodium Citrate	7.15	.02	3.64	.65	3.41	.25
Sodium Acetate	6.82	7.0	3.51	.075	3.47	9.0
Sodium Carbonate	7.71	.1	3.46	.5	3.43	.75
Sodium Bicarbonate	7.31	.3	3.67	.85	3.52	.05
Average pH	7.19		3.62		3.44	
Beginning PPt.						

As shown in the table, the average precipitation point of the hydrochloride is at a pH of 7.19, the dihydrochloride 3.62, and the bisulphate 3.46. It will be noted that these values are in almost the same relation as the pH values of their aqueous solutions. A 2% solution of quinine hydrochloride was found to have a pH of 6.1, dihydrochloride 2.6 and bisulphate 2.4. It will be also noted that the pH figures all lie within the pH ranges of the human stomach and duodenum, as reported by McClendon,³ Hume, Denis, Silverman and Irwin,⁴ and others.

Qualitative determinations on the precipitates showed that they were quinine salts corresponding with the precipitating alkaline salt, *viz.*, quinine acetate, phosphate, carbonate, etc. With NaOH the precipitate was quinine base. The process was apparently stoichiometric.

The results of this work so far would seem to justify the statement that physiological concentrations of alkalis definitely alter the solubility of amounts of quinine salts corresponding to the full therapeutic dose as found in the upper gastro-intestinal tract.

² Michaelis, Leonor, *Praktikum der physikalischen Chemie insbesondere der Kolloidchemie für Mediziner und Biologen*. Berlin, 1926.

³ McClendon, J. F., *Proc. Nat. Acad. Sci.*, 1921, xv, 347.

⁴ Hume, H. V., Denis, W., Silverman, D. N., and Irwin, E. L., *J. Biol. Chem.*, 1924, lx, 633.