Reprinted from the PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE,
1929. xxvi. pp. 541 542

4424

The Effect of Alkalis Upon the Solubility of Quinine Salts.

A. J. HOCKETT. (Introduced by C. H. Thienes.)

From the Department of Pharmacology, University of Oregon Medical School, Portland, Oregon.

The present study was suggested by the paper by Eggleston[1] 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 Michaelis[2] one-color series without buffers, and these values checked by the quinhydrone electrode.

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.

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

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

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 Beginning PPt.	7.19		3.62		3.44	

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 preciptate was quinine base. The process was apparently stoechiometric.

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.

[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.