

TABLE VI.—AMINO-ALCOHOLS AND CORRESPONDING KETONES.

Product.	Precipitate Formations.											Reagent Number.					
	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.
Propadrin												b					
Propadrone					yw	w						b					
<i>o</i> -Methyl-propadrone								b	y			b		w		w	
<i>m</i> -Hydroxy-propadrin					w	w						b					
<i>m</i> -Hydroxy-propadrone						w						b					
<i>m</i> -Hydroxy, <i>p</i> -methylpropadrin												b					
<i>m</i> -Hydroxy, <i>p</i> -methylpropadrone												b					w

TABLE VII.—AMINO-ALCOHOLS AND CORRESPONDING KETONES.

Product.	Color Reaction.											Reagent Number.					
	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.
<i>m</i> -Hydroxy-propadrin		y	y									pb					
<i>m</i> -Hydroxy-propadrone		y	y									pb					
<i>m</i> -Hydroxy, <i>p</i> -methylpropadrin		y										bl					
<i>m</i> -Hydroxy- <i>p</i> -methylpropadrone		y										p					

BIBLIOGRAPHY.

- (1) Walter H. Hartung, "Epinephrine and Related Compounds; Influence of Structure on Physiological Activity," *Chem. Reviews*, 9 (1931), 389-465.
- (2) Walter H. Hartung and James C. Munch, "Amino Alcohols. I. Phenylpropanolamine and para-Tolylpropanolamine," *J. A. C. S.*, 51 (1929), 2262-2266.
- (3) Walter H. Hartung, James C. Munch, W. Allan Deckert and Frank Crossley, "Amino-Alcohols. II. Homologs and Analogs of Phenylpropanolamine," *J. A. C. S.*, 52 (1930), 3317-3322.
- (4) Walter H. Hartung, James C. Munch, Ellis Miller and Frank Crossley, "Amino Alcohols. VII. Phenolic Arylpropanolamines," *J. A. C. S.*, 53 (1931), 4149-4160.
- (5) James C. Munch, Frank C. Crossley and Walter H. Hartung, "Alkaloidal Reagents. I. Introduction," *Jour. A. Ph. A.*, 20 (1931), 1037-1041.
- (6) James C. Munch, Frank C. Crossley and Walter H. Hartung, "Alkaloidal Reagents. II. Aromatic Monohomocyclic Derivatives," *Jour. A. Ph. A.*, 21 (1932), 341-349.

THE LOCAL REACTIONS PRODUCED BY INTRAMUSCULAR INJECTION OF SOME ANTIMONY COMPOUNDS.*

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Very little information is available concerning the physiological behavior of colloidal metallic antimony, sodium antimony iodide or antimony quinine iodide. In view of the fact that a number of antimony compounds such as tartrates, substituted phenylstibinic acids, derivatives of polyhydroxyphenols and of thio-glycollic acid are either essential or of great value in the treatment of kala-azar, bilharziasis, leishmanioses and other protozoal infections, it appeared worth while to determine whether or not a colloidal antimony aqueous solution and sodium antimony iodide or antimony quinine iodide in ethylene glycol solution could be safely used in therapy. Knowledge regarding the biological behavior of these antimonials is also desirable for comparison with the behavior of analogous bismuth compounds. Solutions of these three substances were injected intramuscularly into

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dogs and particular attention was paid to the local reactions which developed. Also the toxicity and absorption of colloidal metallic antimony was studied. The nature of these preparations and the results obtained with them are described here.

COLLOIDAL METALLIC ANTIMONY.

The colloidal metallic antimony was prepared by a method which is essentially the same as that described by Gutbier and Kräutle (1), Usher (2), Gutbier, Ottenstein, and Allam (3) and Fouard (4). A completely reversible colloid containing 7.73% of metallic antimony was obtained. This was made up in aqueous solutions containing 15.5 mg. of antimony per cc., 7.7 mg. of antimony per cc. and 3.9 mg. of antimony per cc., respectively. The solutions were injected intramuscularly into dogs to observe the local reactions produced and into rats to determine the rate of absorption and toxicity.

Five intramuscular injections in four dogs produced marked swelling at the site of injection followed by a generalized swelling throughout the leg injected and finally abscess formation. The muscles were congested and hemorrhagic and the animals suffered considerable pain. The reactions were very severe in every instance. When injected intramuscularly into rats the local reactions were again severe but absorption appeared to be complete within 48 hours. The dose required to kill 50% of the injected rats was 20 mg. of antimony per kilo. When injected intramuscularly and 16.5 mg. per Kg. when injected intravenously. The toxicity was about twice that of sodium antimony tartrate and the local reactions produced were too severe for a compound useful in therapy.

ANTIMONY IODIDE.

The preparation of antimony iodide is described by a number of investigators which are referred to by Mellor (5) so that they will not be mentioned individually here. Antimony iodide was prepared for this investigation by the following process. A saturated solution of antimony trichloride was prepared in ethyl acetate. This solution was then treated with an excess of sodium iodide added in small portions, shaking the solution vigorously after each addition of sodium iodide. The mixture was then filtered to remove excess sodium iodide and sodium chloride. The clear red solution containing the antimony compound was evaporated to dryness *in vacuo* over sulphuric acid. The dry power obtained contained 27.5% of antimony compared to a theoretical antimony content of 23.94% for SbI_3 due to the presence of some antimony oxyiodide. A solution of this compound in ethylene glycol was prepared using 5 Gm. of antimony iodide and 10 Gm. of sodium iodide in 50 cc. of ethylene glycol. Each cubic centimeter of solution contained 25.7 mg. of antimony per cc. The clear red solution so obtained was injected intramuscularly into dogs.

Two intramuscular injections of $\frac{1}{2}$ cc. each of this solution diluted with an equal volume of ethylene glycol, a total of 12.8 mg. of antimony for each injection, were given to each of two dogs. The local reactions were most severe. There was local sensitiveness and considerable pain followed by a local lump formation at the site of the injection and great swelling of the lower part of the leg. Finally an abscess formed with a punched out ulcer and drainage of a hemorrhagic exudate. Control injections of ethylene glycol produced no local reactions whatever so that the severity of the local reactions obtained with this antimony compound were due

solely to the antimony compound and not to the solvent. The results demonstrate clearly that the compound is unsuitable as a therapeutic agent.

ANTIMONY QUININE IODIDE.

Antimony quinine iodide was prepared in a manner similar to that described by many investigators for bismuth quinine iodide, 4.5 Gm. of antimony trichloride were dissolved in 600 cc. of water and 200 cc. of concentrated hydrochloric acid. This solution was then added to a solution of 30 Gm. of sodium iodide and 6 Gm. of quinine hydrochloride in 600 cc. of water. A yellow precipitate was formed which was collected on a Buchner funnel, thoroughly washed with water, and then dried *in vacuo* over phosphoric anhydride. The dry powder contained 9.75% of antimony. A solution of this compound in ethylene glycol was prepared by dissolving 10 Gm. of compound and 20 Gm. of sodium iodide as a stabilizer in 100 cc. of ethylene glycol. The resulting clear red solution contained 11.6 mg. of antimony per cc. The results of intramuscular injection of this solution are as follows:

A single injection of 1 cc. of this solution was made in each of two dogs. The results were similar to those obtained with sodium antimony iodide. The injections cause marked local sensitiveness and considerable pain. This was followed by local lump formation, and tremendous swelling with extension through the injected leg. Subsequently there was abscess formation and a punched out ulcer as before. The reactions were as severe as in the case of sodium antimony iodide and show that this compound, too, is useless as a therapeutic agent.

The severe local reactions produced by all three compounds described here are sufficient evidence that they are not safe therapeutic agents. This is directly opposite to the results which have been obtained with analogous bismuth compounds. Bismuth quinine iodide has long been used in oil suspension or aqueous suspension in syphilis therapy without severe local reactions and bismuth metal in finely divided aqueous suspension or as a colloid does not cause local reactions. In similar studies with ethylene glycol solutions of bismuth iodide complexes local reactions were absent. The great difference between the antimony and bismuth compounds is surprising in view of the great chemical similarity of these two elements which are closely related in the same group of the periodic system. The results show clearly the impossibility of drawing conclusions regarding the most satisfactory means of administering a metal in therapy from results obtained with another metal no matter how closely the two may be related chemically.

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REFERENCES.

- (1) Gutbier and Kräutle, *Kolloid Zeit.*, 20 (1917), 194.
- (2) Usher, *Jour. Soc. Chem. Ind.*, 38 (1919), 98R.
- (3) Gutbier, Ottenstein and Allam, *Zeit. anorg. allgem. Chem.*, 164 (1927), 287.
- (4) Fouard, *Compt. Rend.*, 184 (1927), 328.
- (5) Mellor, "A Comprehensive Treatise on Inorganic and Theoretical Chemistry,"

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