AN UNUSUAL ALKALOIDAL PRECIPITANT.*

BY WILLIAM G. TOPLIS.

Potassium citrate is a remedy of frequent use in prescription work. In the course of years of observation some curious phenomena were noted in connection with potassium citrate that encouraged a closer scrutiny of its behavior.

If, for example, Camphorated Tincture of Opium is saturated with potassium citrate, several changes occur.

First, the alcoholic and watery portions separate into two layers, the lower being a saturated solution of potassium citrate and the water-soluble components of paregoric, the upper layer containing the alcohol and the parts soluble in it. Between the two layers appears, on standing, a precipitate which contains among other things the alkaloids formerly present in the sample. Similar changes occur under like conditions with Tincture of Nux Vomica, Tincture of Cinchona, Tincture of Belladonna, and others.

Precipitates obtained in this manner suggested the possibility of the presence of alkaloids, though they were always colored by matter from the original drug. In order to discover the truth concerning this surmise, a concentrated alcoholic extract of *Cinchona Calisaya* was saturated with potassium citrate. The resulting precipitate was collected upon a filter, thoroughly washed with distilled water, drained, and then treated with dilute hydrochloric acid. The acid filtrate was permitted to evaporate spontaneously, with no attempt at further purification. The result was a crop of colored crystals of the hydrochlorides of the mixed alkaloids of cinchona.

To prove this statement, further work with crude drugs was abandoned, and the next step was a study of the behavior of potassium citrate with known alkaloids taken from stock. Accordingly, it was found that quinine bisulphate, in distilled water, is promptly and completely precipitated by potassium citrate. The nature of this precipitate was not known positively until, after thorough washing with distilled water to remove sulphates, a final test disclosed the precipitate to be quinine citrate. This test was carried out by the use of an immiscible solvent (ether, alcohol, ammonia) upon the wet precipitate on the filter. The ethereal portion contained the quinine in solution, as a supernatant layer of the filtrate, while the watery portion held the citric acid as ammonium citrate. It was from this portion that a satisfactory test for citric acid was obtained.

Citrate of quinine is only sparingly soluble in water; a portion after repeated washing showed little loss of weight. Its solubility is probably not greater than that of quinine alkaloid, which is reported to be 1 in 1,500 parts of water. Citrate of quinine is even less bitter to taste than quinine alkaloid. It seems that the quinine citrate may be precipitated quantitatively by an excess of the reagent and, perhaps, serve as an easy assay method.

Quinine citrate is readily soluble in dilute hydrochloric acid, and, therefore, doubtless capable of its physiological action in the system, after conversion in the stomach. Sodium citrate behaves in the same manner, so far as precipitating alkaloid is concerned, but it does not separate the alcohol from the water in tinctures as does potassium citrate. We have found that the alkaloids of opium, nux vomica,

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cinchona, belladonna and, doubtless, others respond to this reagent, in fact so far as we have gone there has been not one exception. All have been precipitated, though not with the same facility, some responding more promptly in dilute solution than others. In this respect quinine seems to be more responsive than all of those examined thus far, probably because of its low solubility.

It was found by experiment that a 5% quinine solution was precipitated with a like amount of potassium citrate. In one instance, in a still more dilute solution, after standing, the quinine appeared in long, colorless needles. Strychnine sulphate, 1% solution, precipitated slowly in the presence of 5% potassium citrate as small, brilliant crystals adhering to the sides of the tube; in a 10% potassium citrate solution the precipitation was rapid and complete. Morphine, 5% solution, was promptly precipitated by 5 percent of potassium citrate. Codeine, heroine, atropine, were all precipitated, and in most instances did not redissolve upon further dilution with water. Caffeine precipitated in concentrated solution but redissolved on further dilution.

These facts suggest the advisability of "shake well" labels on prescriptions containing such ingredients.

The foregoing is all we have to offer so far as demonstrable truth is concerned. In addition, however, we invite you to go with us on a short excursion through a fanciful speculation. Alkaloids are nitrogenous bodies that form addition compounds like ammonia; amines behave similarly; ptomaines derived from putrefactive changes in intestinal contents; toxins derived from the development of bacteria in favorable culture media, and venom from poisonous reptiles are, if we are correctly informed, similar in composition to alkaloids.

Potassium citrate is described in the U. S. Dispensatory as being diaphoretic and refrigerant. There is no statement as to how its functions are performed and it is doubtful whether this information is known.

The question that naturally arises in light of the above statements is, does potassium citrate, when absorbed into the circulation, encounter therein toxic substances, and does it unite with them to form insoluble compounds, as in the test tubes? And further, if this surmise should prove to be true, would it follow that former poisons would become inert? And if this should prove to be true, would it not follow that the logical manner for introducing the remedy into the system would be by way of intravenous injection? And in light of the fact that sodium compounds are best tolerated by the system, would not a sterilized solution of sodium citrate be the proper mode of administration?

We have very little experimental evidence to offer in support of this theorizing. Just one little fact is worthy of mention: Hexamethylenamine gives a very finely divided precipitate in presence of potassium citrate.

ABSTRACT OF DISCUSSION.

In answer to a question by Dr. C. B. Lowe as to how long it required for precipitation to occur, the author answered—"immediately."

Charles H. LaWall said, "It is certainly interesting that a hitherto unrecorded fact should now be presented relative to a frequently used remedial agent, that is an alkaloidal precipitant. It really comes with added force that the 'Shake well' label should be more frequently used."