Contributed and Selected

A PROCESS OF ASSAY FOR SANGUINARIA.*

V. O. HOMERBERG, P. D., AND G. M. BERINGER, JR., P. D.

Often, the mind of human science travels in a mental maze, taking its turns by guess or luck, blindly ignoring the pointing finger on nature's sign-post. To most, if not all of her riddles nature herself furnishes the key. The assay of Sanguinaria Canadensis, and the problems involved in the search for that assay, furnish striking proofs of these two propositions. Few alkaloidal assays present so many difficulties.

The strong colors of the salts of the principal alkaloids preclude the use of any volumetric process, as no indicator and no end reaction would be available in their presence. In the separation of the alkaloids from the drug, the soluble alkalies—soda, potash and ammonia—precipitate the coloring matter along with the alkaloids, which coloring matter later forms troublesome emulsions with the solvents. Kieselguhr and kaolin were tried for removing the coloring matter, but were found to retain considerable of the alkaloids. Finally, lime was found to liberate the alkaloids, and, at the same time retain the coloring matter.

Many of the volatile solvents, upon evaporation, leave the dissolved sanguinaria alkaloids decidedly colored. This is true especially of acetic ether and chloroform, traces of these solvents being apparently decomposed, thus giving enough free acids to salify a portion of the alkaloids. Chloroform is evidently the best solvent for the mixed alkaloids, but cannot be used upon this account. The next best solvent seems to be benzol, but it takes up large quantities of coloring matter. The only two solvents free from this objection are benzin and ether. Benzin, however, as shown by LaWall (Am. Jr. Ph., '96, p. 305, et seq.) dissolves only a part of the alkaloids. Ether dissolves them all, but is required to be used in larger amount than benzol because of its weaker solvent action. The final solution of this problem was the use of ether for the first extraction, thus leaving behind practically all of the coloring matter, and the use of benzol for the final extraction, thus giving a smaller bulk for evaporation.

The greatest trouble is met, however, in trying to extract the alkaloids from the ethereal solutions by means of acid solutions. The mineral acids, even in dilute solutions, precipitate a large part of the alkaloids. It has been this, no doubt, which has rendered most previously published assays uncertain and unreliable. The alkaloids evidently existed in combination in the plant. With what natural acids are they combined? Almost thirty years ago, L. C. Hopp (Am. Jr. Ph., '75, p. 183, et seq.) demonstrated by simple but conclusive tests that those

*Presented to the N. J. Pharmaceutical Association, June 1913.

acids were citric and malic acids. But, the question arose, would not the volatile solvents extract some of the sodium citrate formed upon neutralization of the acid solutions with sodium hydroxide? In order to determine this, sodium citrate was treated in separate portions with ether and benzol. Upon evaporation of the filtered solvent in a platinum basin no weighable residue was left in the case of benzol, and only a slight residue in the case of ether. Hence, using the two solvents in the order finally adopted in the perfected assay, the results were not vitiated by the presence of citrates.

Many experiments and scores of unsuccessful assays were necessary to determine the facts given above. From them the following assay was evolved:

Gradually add seven cubic centimeters of water to two grams of air-slaked lime contained in a suitable dish. To the magma thus formed, add two grams of finely powdered sanguinaria and incorporate thoroughly. Evaporate on a water bath to dryness. Transfer the dry material, after powdering, to a small percolator, the orifice of which has been closed with a pledget of paper pulp, moistened with a mixture of equal volumes of ether and benzol. Rinse the dish with a few cubic centimeters of the same ether-benzol mixture and pour the rinsings upon the material contained in the percolator. Continue the percolation by the addition of small portions of the ether-benzol mixture from time to time until a drop of the percolate, evaporated in a watch crystal and redissolved by the addition of one drop of diluted hydrochloric acid, no longer gives a precipitate with Mayer's reagent. Transfer the percolate to a separatory funnel and wash with separate portions of solution of citric acid (5%) of 25 cc., 15 cc. and 10 cc. respectively. Continue the treatment with portions of 5 cc. of the acid solution till one drop of the acid solution shows no precipitate with Mayer's reagent.* Transfer the mixed acid solutions to a separatory funnel, add 15 cc. of benzol and afterward sufficient sodium hydroxide solution to make the mixture alkaline to litmus. Shake the mixture thoroughly. Separate and filter the benzol layer into a tared beaker. Repeat the operation with two portions of 10 cc. each of benzol, mixing the separated and filtered benzol solutions with that first obtained. Evaporate the mixed solutions, on a water-bath, to dryness. Cool the beaker and residue in a desiccator and weigh. The commercial drug at present assays from 3-4% total alkaloid.

For assaying the Tincture and Fluidextract, take 20 cc. and 2 cc. respectively and evaporate the alcohol on a water-bath; mix with the lime magma and proceed as above.

The residues given by this method are practically white and crystalline. Results are remarkably constant as compared with previous assays, the weights rarely varying more than .001 in assaying the same sample.

NOTE.—The work embodied in this paper was carried out by Victor O. Homerberg and presented by him in a thesis, for his degree, before the Philadelphia College of Pharmacy. His associate has merely rewritten this portion for presentation to this Association.

G. M. B., JR.

*Total extraction of alkaloid is generally shown by absence of color in the Citric Acid Solution.