

Fig. 7.—Ephedrine Salted out with Sodium Chloride.

tungstic acid and zinc-chlor-iodide. A nitrous acid test was not successful, probably due to rapid dissipation of the acid at room temperature. Million's reagent, also reported as a precipitating reagent (15), formed clear solutions with samples tested, no crystalline precipitate being obtained even on long standing. The orange precipitate of the osmic acid color test (14) was examined microscopically but appeared to consist entirely of amorphous masses.

SUMMARY AND CONCLUSION

The authors have presented a review and discussion of tests for *l*-ephedrine and its salts and a laboratory survey of microchemical tests for this alkaloid, from which the following conclusions may be drawn:

1. Numerous acceptable tests for ephedrine have already been devised. Of these, the color and microscopic methods seem to offer the best means of identification.
2. The U. S. P. XI biuret reaction and the osmic tetraoxide reagent seem to give the best color tests.
3. Microcrystalline precipitates form slowly in ephedrine test drops, but identification may be made through the micro tests with Dragendorff's Reagent, platonic chloride reagent and potassium oxalate.
4. A combination of these tests may be used to distinguish *l*-ephedrine from ephedronin, the pseudo-ephedrine and adrenaline.

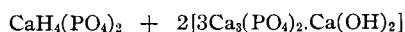
REFERENCES

- (1) Chen, K. K., and Schmidt, C. F., *Proc. Soc. Exptl. Biol. Med.*, 21 (1923-1924), 351.
- (2) May, Percy, and Dyson, G. M., "The Chemistry of Synthetic Drugs" (1939), page 164, Longmans Green & Co., London.
- (3) Chen, K. K., *Chemist and Druggist*, 129 (1938), 585.
- (4) Lum, E. A., *Mfg. Chemist*, 8 (1937), 65.
- (5) Henry, T. A., "Plant Alkaloids" (1939), page 562, P. Blakiston and Son, Philadelphia.
- (6) Rosenthaler, L., "Toxicologische Mikro-analyse" (1936), page 257, Borntrager Bros., Berlin.
- (7) Pharmacopœia of the United States, Eleventh Revision (1936).
- (8) Moore and Tabern, *JOUR. A. PH. A.*, 24 (1935), 211.
- (9) American Drug Manufacturers Association, *Proceedings*, 24 (1935), 135, 251.
- (10) Sanchez, J. A., *J. pharm. chim.*, 22 (1935), 489; from *Squibb Abstr. Bull.*, 9 (1936), 186.
- (11) Chen, K. K., *JOUR. A. PH. A.*, 18 (1929), 110.
- (12) Pesez, M., *J. pharm. chim.*, 27 (1938), 120-128.
- (13) Eckkert, M., *Ibid.*, 22 (1935), 168.
- (14) Fourment, P., and Roques, H., *Bull. sci. pharmacol.*, 44 (1937), 372; from *Squibb Abstr. Bull.*, 10 (1937), 1752.
- (15) Tsiang, K., and Brown, E. D., *Bull. sci. pharmacol.* 16 (1927), 294.
- (16) Feng, C. T., and Brown, E. D., *Ibid.*, 22 (1933), 124.
- (17) *J. Assoc. Off. Agr. Chem.*, 14 (1931), 316.
- (18) Paris, G. A. W. G. O. E., *Pharm. Weekblad*, 73 (1936), 1526; from *Squibb Abstr. Bull.*, 9 (1936), 1890.
- (19) A. O. A. C., "Methods of Analysis" (1935), page 557.
- (20) Garrett, D. C., "Drugs and Galenicals" (1927), Chapman-Hall, London.

A Study of the Composition of Precipitated Calcium Phosphate National Formulary VI*

By J. W. Millar

The formula given in National Formulary VI for Precipitated Calcium Phosphate is $\text{Ca}_3(\text{PO}_4)_2$ and the same formula is given in the French Codex for "Neutral Calcium Phosphate." The British Pharmacopœia gives no formula, but Bennett and Cocking (1) attribute the following formula to the salt of the British Pharmacopœia:

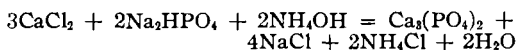


* Contribution from the Laboratories of the College of Pharmacy, University of California, Medical Center, San Francisco, California.

The salt is not official in the German Pharmacopœia.

Mellor (2) and others (3) apparently doubt the correctness of the formula given in N. F. VI, Mellor stating that "Strictly normal Calcium Phosphate has not been prepared in the wet way."

The equation of formation of the salt where shown in texts (4) is:



The formula given in the National Formulary VI, namely, $\text{Ca}_3(\text{PO}_4)_2$ with a molecular weight of 310.28, gives a theoretical composition: Ca 38.75 per cent and PO_4 61.24 per cent. These results were not obtained in any of the analyses carried out in this laboratory, the results for calcium being invariably higher and for phosphate lower than the above theoretical values.

The formula given by Bennett and Cocking (1), $\text{CaH}_4(\text{PO}_4)_2 + 2[3\text{Ca}_3(\text{PO}_4)_2 \cdot \text{Ca}(\text{OH})_2]$, gives a theoretical composition: 38.09 per cent, PO_4 60.19 per cent, and shows the presence of 10.59 per cent of mono-calcium-ortho phosphate, $\text{CaH}_4(\text{PO}_4)_2$, a soluble salt.

Table I.—Comparison of Results Found with Those Computed

	N. F. VI $\text{Ca}_3(\text{PO}_4)_2$ M. W. 310.28	B. & C. (1) $\text{CaH}_4\text{PO}_4 +$ $[23\text{Ca}_3(\text{PO}_4)_2 \cdot$ $\text{Ca}(\text{OH})_2]$ M. W. 2209.96	Suggested $[\text{Ca}_3(\text{PO}_4)_2]_3 \cdot$ $\text{Ca}(\text{OH})_2$ M. W. 1012.14	Results Obtained, Average
Ca	38.75	38.09	40.31	40.12
PO_4	61.24	60.19	56.33	56.43
O (calculated)	...	0.72	1.57	1.57
H_2O from $\text{Ca}(\text{OH})_2$ on ignition	...	0.81	1.78	1.83
H in $\text{CaH}_4(\text{PO}_4)_2$...	0.18
Total	99.99	99.99	99.99	99.95

From the analysis carried out in this laboratory, the possibility of a basic salt became apparent and the following formula is suggested:



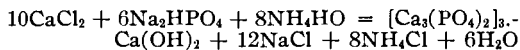
which has the following theoretical composition:

Ca	40.31 per cent
PO_4	56.33 per cent
$(\text{OH})_2$	3.37 per cent

or calcium combined with

PO_4	35.88 per cent
PO_4	56.73 per cent
$\text{Ca}(\text{OH})_2$	7.37 per cent

An equation for the formation of a basic salt may be shown as:



This basic salt may be converted at high temperature to $[\text{Ca}_3(\text{PO}_4)_2]_3 \cdot \text{CaO}$ giving a theoretical composition of:

Ca	40.31 per cent
PO_4	56.33 per cent
O (combined as CaO)	1.57 per cent
	<hr/> 98.21 per cent
Water (due to conversion of $\text{Ca}(\text{OH})_2$ to CaO)	1.78 per cent
	<hr/> 99.99 per cent

EXPERIMENTAL

All samples of the salt analyzed conformed with the tests for purity listed in N. F. VI; and no appreciable residue was obtained when the salt was well shaken with water and the filtrate evaporated to dryness.

The two samples used for analysis were obtained from commercial sources; number one labeled "Calcium Phosphate—Tribasic—Precipitated P-W-R," number 2 labeled "Calcium Phosphate Merck—Tribasic—Precipitated."

Samples were dried at 200° C. to constant weight.

The analytical method used for phosphorus was: precipitation as ammonium phospho-molybdate; the precipitate dissolved in ammonia; phosphate precipitated with magnesia mixture. Weighed as magnesium pyro-phosphate (5). The calcium was precipitated as oxalate with ammonium oxalate and converted to calcium carbonate by careful ignition at 500° C. ($\neq 10^\circ$ C.).

The monograph in National Formulary VI states that, "When dried to constant weight at 200° C., the salt loses not more than 4 per cent in weight (water)."

Pure calcium phosphate is unaffected by heat up to 1670° C. (6). Calcium hydroxide loses water at 580° C.

The samples analyzed lost (av.) 3.76 per cent in weight when heated at 200° C. to constant weight; and at a temperature of 1500° C. for two hours lost a further 1.83 per cent, apparently not due to hygroscopic moisture.

SUMMARY

From the analytical results obtained it appears that the formula for precipitated calcium phosphate, $\text{Ca}_3(\text{PO}_4)_2$, given in the National Formulary VI and in the French Codex are in error.

It also appears that the formula suggested $[\text{Ca}_3(\text{PO}_4)_2]_3 \cdot \text{Ca}(\text{OH})_2$ more closely agrees with the true composition of the salt.

REFERENCES

- (1) Bennett and Cocking, "Science and Practice of Pharmacy," Vol. 2 (1933), page 102, Churchill.
- (2) Mellor, "Treatise on Inorganic Chemistry" (1925), page 725, Longmans-Green.
- (3) *American Pharmaceutical Pamphlets*, 3 (1939), 319.
- (4) Rogers, "Inorganic Pharmaceutical Chemistry" (1936), page 360, Lea and Febiger.
- (5) Kolthoff and Santell, "Quantitative Inorganic Analysis" (1938), pages 324, 367, Macmillan.
- (6) Lange, "Physical Constants," 2nd Edition, page 132, Hand Book Publications, Inc.

Pharmaceutical Emulsions. III. A Comparative Study of Various Mechanical Stirrers and the Hand Homogenizer*[†]

By William J. Husa[‡] and Charles H. Becker**

INTRODUCTION

In earlier papers (1, 2) detailed studies were made of the Continental and English methods of emulsification. The present

* Presented before the Scientific Section, A. Ph. A., Richmond meeting, 1940.

[†] This paper is based on part of a thesis presented to the Graduate Council of the University of Florida in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[‡] Head Professor of Pharmacy, University of Florida.

** Graduate Scholar, University of Florida, 1939-1940.

investigation is devoted to a study of the efficiency of these older methods of emulsification as compared with the use of mechanical stirrers and a homogenizer for making emulsions.

EXPERIMENTAL

Materials.—The stirrers used were: (a) motor stirrer, with a glass stirring rod, maximum speed about 3000 r. p. m., purchased from the Central Scientific Co., (b) Arnold automatic mixer, intended for use at the soda fountain, (c) hand egg beater. A portable hand homogenizer, purchased from the International Emulsifiers, Inc., was employed.

The fixed oils chosen for study were linseed oil, cod liver oil, heavy mineral oil and castor oil. All the oils were of U. S. P. grade. Powdered acacia, U. S. P., was employed. One-tenth per cent sodium benzoate was added to the distilled water to prevent mold growth in the emulsions while standing for observation. *Methods.*—The general methods employed were the same as described in previous papers (1, 2).

Throughout, the parts of acacia were measured in Gm. and the parts of oil and water were measured in cc.

In the tables "oil sep." is used to indicate oil separation. The following abbreviations are used to indicate the average size of the oil globules:

- A—Average diameter less than 2.5 microns.
- B—Average diameter from 2.5 to 4 microns.
- C—Average diameter from 4 to 6 microns.
- D—Average diameter more than 6 microns.

Use of Motor Stirrer.—Four-ounce portions of 12½% oil emulsions were prepared using the 4:2:1 proportion. In all cases the stirring was conducted at maximum speed. The emulsions were prepared in the following ways:

Method I: The 4 parts of oil and 1 part of acacia were first mixed well in a 150-cc. beaker with the motor stirrer, and then the 2 parts of water was added all at once. The primary emulsion was stirred for 5 minutes, and the remainder of the water was added gradually.

Method II: The primary emulsion was first made using a porcelain pestle, 15.0 cm. in length and 4.5 cm. in diameter at the base, and a No. 1 wedgwood mortar, and then this was transferred to a 150-cc. beaker and stirred for 5 minutes. The remainder of the water was added gradually.

Mineral oil did not yield an emulsion when made according to the procedure described in Method I. With cod liver oil and linseed oil, the motor stirrer appeared to be of little value, inasmuch as 5 minutes of stirring yielded emulsions which were equivalent, with respect to the average size of the oil globules, to products wherein the primary emulsion was triturated in a mortar for 1 minute. Castor oil yielded a Grade A emulsion.