

- Fleury, P.  
**Action of mercury salts on veronal. Some analytical applications**  
*J. pharm. chim.*, 2 (1925), 465
- Funk, C.  
**An attempted classification of the vitamins**  
*Bull. soc. chim. biol.*, p. 1017; through *J. pharm. Belg.*, 7 (1925), 837
- Glaser, E. and Halpern, G.  
**Chemical composition of insulin**  
*Biochem. Z.*, 101 (1925), 1; through *J. pharm. Belg.*, 7 (1925), 840
- Guyot, R.  
**Color reactions of adrenaline**  
*Bull. soc. pharm. Bordeaux*, 4 (1925), 214
- Mannich, C. and Curtaz, K.  
**Contribution to the knowledge of silver albuminoids**  
*Arch. Pharm.*, 9 (1925), 669
- Maschmann, E.  
**Notes on bismuth compounds. II**  
*J. Russ. Phys.-Chem.*, 48 (1916), 324; through *Arch. Pharm.*, 9 (1925), 721
- Newcomb, C.  
**Determination of alcohol and ethyl chloride in chloroform**  
*Chem. & Drug.*, 103 (1925), 892
- Olszewski, B.  
**Methyl alcohol test**  
*Roszniki Farmacji*, No. 1-2, vol. 3; through *Chem. & Drug.*, 103 (1925), 891
- Parri, W.  
**Color reaction of veronal**  
*Boll. chim.-farm.*, (1924), 401; through *Répert. pharm.*, 36 (1925), 340
- Penfold, A. R.  
**Identity of uncineol with eudesmol**  
*J. Roy. Soc. N. S. Wales* (July 1, 1925); through *Perf. & Ess. Oil Rec.*, 16 (1925), 450
- Reif, M. G.  
**Estimation of dulcin by means of xanthidrol**  
*Zeit. Unters. Nahr. Genussm.*, 47 (1924), 238; through *J. pharm. chim.*, 2 (1925), 493
- Rothwell, C. S.  
**Direct precipitation of calcium in milk**  
*J. Biol. Chem.*, 65-I-S (1925), 129; through *Schweiz. Apoth. Ztg.*, 63 (1925), 703
- Schoorl, N.  
**Stability of calcium acetylsalicylate**  
*Pharm. Weekbl.*, 62 (1925), 1166; through *Chem. Abstr.*, 20 (1926), 90

## ACCURACY OF HYPODERMIC TABLETS.

The degree of accuracy with which hypodermic tablets should comply with their declared compositions is outlined in a ruling under the Federal Food and Drugs Act issued October 22nd by the Bureau of Chemistry, United States Department of Agriculture. The text of the ruling follows:

Within the last few years the Bureau of Chemistry, in the enforcement of the Food and Drugs Act, has given particular attention to medicinal tablets, especially the more commonly used hypodermic tablets. The data thus collected show that most tablets on the market comply reasonably well with the compositions declared. A material number, however, were found to vary from the stated compositions by amounts in excess of what should be expected under properly controlled conditions of manufacture.

These preparations are of prime importance medicinally. They are manufactured from physiologically potent substances and constitute the chief dependence of the physician in emergencies. The physical characteristics of a hypodermic tablet usually furnish no information as to its quantitative composition. Physicians, druggists, and patients must rely upon the label. Serious consequences may follow any misstatement.

The Bureau of Chemistry will regard as adulterated or misbranded, or both, those hypodermic tablets which fail to comply with declared compositions to an extent greater than occurs in such tablets manufactured under properly controlled processes. In ascertaining the degree of accuracy practicable careful consideration will be given to the conclusions of committees representing the drug manufacturing industry which have studied this question thoroughly and have presented a comprehensive report to the Bureau of Chemistry. These committees have suggested the maximum variations, either above or below the labeled or claimed amounts (including all tolerances), which in their opinion should be permitted in tablets manufactured under properly controlled processes. They are as follows:

	Per cent.
Atropine sulphate hypodermic tablets purporting to contain $\frac{1}{4}$ gr. or more	7.5
Atropine sulphate hypodermic tablets purporting to contain less than $\frac{1}{4}$ gr.	9.0
Cocaine hydrochloride hypodermic tablets	9.0
Codeine sulphate hypodermic tablets	9.0
Morphine sulphate hypodermic tablets	7.5
Strychnine sulphate hypodermic tablets purporting to contain $\frac{1}{4}$ gr. or more	7.5
Strychnine sulphate hypodermic tablets purporting to contain less than $\frac{1}{4}$ gr.	9.0
Strychnine nitrate hypodermic tablets purporting to contain $\frac{1}{4}$ gr. or more	7.5
Strychnine nitrate hypodermic tablets purporting to contain less than $\frac{1}{4}$ gr.	9.0

#### METHODS OF ANALYSIS RECOMMENDED BY COMMITTEES REPRESENTING THE INDUSTRY.

The committees representing the manufacturing industry recommend the following methods of analysis of the products mentioned above. The Bureau of Chemistry, for the analysis of official samples, employs methods based upon the same general principles as those given below, although some of the details of the procedures may vary somewhat. Studies of these methods show that they give results which agree satisfactorily with those used by the Bureau of Chemistry.

These methods have been referred to the referee on drugs of the Association of Official Agricultural Chemists for his consideration or further study by that association.

#### HYPODERMIC TABLETS—ATROPINE SULPHATE.

In case of tablets containing  $\frac{1}{20}$  grain of atropine sulphate or in excess of this amount, dissolve at least 20 tablets in sufficient distilled water to make 100 cubic centimeters and take an aliquot equal to at least one grain of atropine sulphate.

In case of tablets containing less than  $\frac{1}{20}$  grain of atropine sulphate, dissolve a sufficient number to represent at least one grain of atropine sulphate in sufficient distilled water to make a clear solution.

In either case make the aqueous solution distinctly alkaline with ammonia and shake out with several portions of chloroform until tests with Mayer's reagent indicate that the aqueous solution has been completely exhausted of the alkaloid. Evaporate the combined chloroform extracts to dryness on the water-bath. Dissolve the residue in a few cubic centimeters of neutral alcohol. Add 10 cubic centimeters of  $N/20$  sulphuric acid and titrate excess of acid with  $N/50$  potassium hydroxide solution, using methyl red indicator.

Each cubic centimeter of  $N/20$  sulphuric acid consumed corresponds to 0.017362 gram of atropine sulphate,  $(C_{17}H_{23}O_3N)_2H_2SO_4 + H_2O$ .

#### HYPODERMIC TABLETS—COCAINE HYDROCHLORIDE.

Dissolve not less than 20 tablets in sufficient distilled water to make 100 cubic centimeters and take an aliquot equivalent to at least one grain of cocaine hydrochloride. Make the aqueous solution slightly alkaline with ammonia and shake out with several portions of ether until the aqueous layer is shown to be completely exhausted of alkaloid, using Mayer's reagent for the test. Combine the ether extracts and evaporate the major portion of the ether on the steam-bath, finally allowing the remainder to be dissipated at room temperature. Dissolve the residue in a few cubic centimeters of neutral alcohol. Add 10 cubic centimeters of  $N/20$  sulphuric acid, and titrate the excess of acid with  $N/50$  potassium hydroxide, using

methyl red indicator. Each cubic centimeter of *N*/20 sulphuric acid corresponds to 0.016983 gram of cocaine hydrochloride,  $C_{17}H_{21}O_4NHCl$ .

#### HYPODERMIC TABLETS—CODEINE SULPHATE.

Dissolve not less than 20 tablets in sufficient distilled water to make 100 cubic centimeters and take an aliquot equivalent to at least one grain of codeine sulphate. Make the aqueous solution alkaline with ammonia and shake out with several portions of chloroform until the aqueous solution is shown to be exhausted of alkaloid, using Mayer's reagent for the test. Evaporate the combined chloroform extracts to dryness on the water-bath, and dissolve the residue in a few cubic centimeters of neutral alcohol.

Add 10 cubic centimeters of *N*/20 sulphuric acid and titrate the excess of acid with *N*/50 potassium hydroxide solution, using methyl red indicator.

Each cubic centimeter of *N*/20 sulphuric acid consumed corresponds to 0.019663 gram of codeine sulphate,  $(C_{18}H_{21}O_3N)_2H_2SO_4 + 5H_2O$ .

#### HYPODERMIC TABLETS—MORPHINE SULPHATE.

Dissolve not less than 20 tablets in sufficient distilled water to make 100 cubic centimeters and take an aliquot equivalent to at least one grain of morphine sulphate. Make the aqueous solution slightly alkaline with ammonia and shake out six times with a mixture consisting of three parts of chloroform and one part of alcohol.

Evaporate the combined extracts to dryness on the water-bath and dissolve the residue in a few cubic centimeters of neutral alcohol. Add 10 cubic centimeters of *N*/20 sulphuric acid and titrate the excess of acid with *N*/50 potassium hydroxide.

Each cubic centimeter of *N*/20 sulphuric acid corresponds to 0.018962 gram of morphine sulphate,  $(C_{17}H_{19}O_3N)_2H_2SO_4 + 5H_2O$ .

#### HYPODERMIC TABLETS—STRYCHNINE SULPHATE OR STRYCHNINE NITRATE.

In case of tablets containing  $\frac{1}{20}$  grain of strychnine sulphate or strychnine nitrate or in excess of this amount, dissolve at least 20 tablets in sufficient distilled water to make 100 cubic centimeters and take an aliquot equal to at least one grain of strychnine sulphate or strychnine nitrate.

In case of tablets containing less than  $\frac{1}{20}$  grain, dissolve a sufficient number to represent at least one grain of strychnine sulphate or strychnine nitrate in sufficient distilled water to make a clear solution.

In either case make the aqueous solution distinctly alkaline with ammonia and shake out with several portions of chloroform until tests with Mayer's reagent indicate that the aqueous solution has been completely exhausted of the alkaloid. Evaporate the combined chloroform extracts to dryness on the water-bath. Dissolve the residue in a few cubic centimeters of neutral alcohol. Add 10 cubic centimeters of *N*/20 sulphuric acid and titrate the excess of acid with *N*/50 potassium hydroxide solution, using methyl red indicator.

Each cubic centimeter of *N*/20 sulphuric acid consumed corresponds to 0.021414 gram of strychnine sulphate,  $(C_{21}H_{22}O_2N_2)_2H_2SO_4 + 5H_2O$ , or 0.01986 gram of strychnine nitrate,  $C_{21}H_{22}O_2N_2HNO_3$ .