The third method is well adapted for examining tablets which contain coloring matter, or pills which contain resins, gums and similar substances. The sodium or potassium oxalate is added to eliminate the hypochlorite which is formed during the reaction and which would cause a precipitation of sulphur when conducting the hydrogen sulphide into the solution obtained. Naturally all insoluble matter should be eliminated by filtration before the mercury is precipitated by the hydrogen sulphide. Calcium phosphate which is frequently applied as a diluent in making tablets of this kind is also precipitated as oxalate.

These methods were applied to mixtures of various composition, and also to various kinds of tablets. The mixtures were the following, the amount of ingredients being expressed in grams. The following results were obtained:—

	Mixture No. 1	Mixture No. 2	Mixture No. 3	Mixture No. 4
Calomel	5 gms.	5 gms.	5 gms.	2.5 gms.
Sod. Bicarb.	5 gms.	10 gms.	25 gms.	2.5 gms.
Starch	1 gm.	2 gms.	5 gms.	5 gms.
Talcum	1 gm.	2 gms.	5 gms.	5 gms.
Glycolene	0.5 gm.	1 gm.	2 gms.	2 gms.
Prec. Calc. Phos. q. s. ad	25	50	100	100
Calomel in Mixtures	20%	10%	5%	2.5%

	Mixture No. 5	Mixture No. 6
Calomel	2.5 gms.	2.5 gms.
Milk Sugar q. s. ad	50 gms.	10 gms.
Calomel in Mixtures	5%	25%

	1	2	3	4	5	6
Method I	99.1%	98.0%	100 %	96 %	99.5%	99.1%
Method II	99.8%	100 %	100.9%	96.7%	99.8%	99.2%
Method III	98.3%	99.6%	97.2%	95.1%	100.1%	100 %

Three kinds of tablets were examined and the results obtained by the three methods represent the following amount of the theoretical amount present:—

Tablets Method I	90 %	94 %	106%
Method II	97.3%	100.1%	98%
Method III	98.2%	101 %	99%

Analytical Laboratory of Sharp & Dohme, July, 1914.

SOME FACTORS IN DRUG ABSORPTION IN FROGS.

W. F. BAKER, M. S., M. D.

Among the objections that have been urged against the frog-heart assay method for the digitalis bodies, the principal ones are the factor of absorption and the time-limit. Of these, the factor of absorption is undoubtedly the more important, the time-limit being dependent upon the rate of absorption.

The manner in which various fluids are absorbed from the lymph sac or the absorption prevented, has not been determined. Experiments and experience have demonstrated, however, that the majority of healthy frogs will absorb from the ventral lymph sac, in a period of one hour, a quantity of fluid equal to about 0.015 cc. per gram of body weight.

Focke has demonstrated that enough of the digitalis bodies may be absorbed in five to twenty minutes to produce the characteristic digitalis heart and has taken twenty minutes as the time-limit for his method. Magnus, using another method, has extended the time to one-half hour, Famulener and Lyons to one hour, and

Houghton to twelve hours. Not infrequently, when assaying preparations by the one-hour method and by the twenty-four method, I have found that out of a series of ten apparently healthy frogs, in not more than one or two frogs would the absorption be complete. At another time, using the same preparation or solution and frogs of the same lot, and under apparently the same conditions, absorption would be complete in every instance. If this non-absorption was but rarely observed, the cause might be attributed to that ever-ready idiosyncrasy. Occurring as it does at times in nearly every member of a series, it appears to be more than an individual peculiarity, and becomes a factor of great importance in this assay method.

While poor absorption may be met with during any time of the year, it is especially likely to occur during the Spring and late Fall. Certain preparations are very prone to meet with poor absorption, as German digitalin, digitoxin and preparations containing acetic acid or glycerin.

In a series of experiments with strychnine and ouabain, frogs placed in these solutions quickly (3 to 15 minutes) absorbed enough of the drug through the skin to produce the typical poisoning. The same results were secured after pithing (brain only for strychnine—brain and cord for ouabain). In another series, in which the solutions were injected into the lymph sac after pithing, complete absorption had taken place within 60 minutes in some frogs, while with others there had been but little absorption. In another series of experiments, a flap was made from the skin of the abdomen, and the drug painted on the under surface of the flap, that is, the lining of the lymph sac, and in others painted on the surface of the abdominal muscles, care being taken to prevent the solution touching the skin. Typical poisoning was produced in all cases except with ouabain on the inner surface of the flap, when in only two instances was the ouabain action observed in a series of twelve experiments. In still another series after pithing, the skin was removed from the hind legs and the frog suspended so that these were in solutions of strychnine or ouabain. The typical poisonings were produced. This did not occur with strychnine if a ligature was previously placed around the base of the heart.

From these experiments it would appear that absorption, of these two drugs at least, may take place from the outer or inner surface of the skin or from the surface of the muscles. The mechanism of absorption or prevention of absorption is not under control of the central nervous system.

Frogs kept in the light appear to absorb better than those kept in the dark. Absorption occurs more readily at higher temperatures, although at a temperature of 30° C., for one hour absorption is not always complete.

It was suggested that perhaps the manner in which the frogs were kept might have something to do with the absorption. Several series of experiments were made upon lots of frogs of testing them as soon as they arrived and again after they had been kept for some weeks under uniform conditions. The main points brought out by this work were, that different lots of frogs varied in their susceptibility to ouabain and digitalis when first received, and some lots absorbed more readily than others.

To determine if the amount of moisture present in the frog influenced absorption, frogs were kept in dry cases until they had lost 10, 25 and 50 *per cent.* of

their weights and then solutions were injected into the lymph sacs. It was found that these frogs absorbed even less readily than the controls kept in wet cages.

In another series of experiments it was found that .9 *per cent.* salt solution was more readily absorbed than distilled water, and 25 *per cent.* alcohol more readily than the salt solution. 50, 75 and 95 *per cent.* alcohol is fairly well absorbed, but not so readily as the 25 *per cent.*

Frogs which are plainly diseased (red-leg disease) may absorb quite readily, while others which, to all appearances are quite healthy, may not absorb at all. In two instances of this kind, I obtained roughly 25 *per cent.* more fluid from the ventrol lymph sac than I had injected. I believe, however, that the matter of absorption is largely due to the health of the frogs and the condition under which they are kept, and if proper attention is paid to the handling, cleansing and storing of the frogs, but little difficulty will be experienced with poor absorption. If, when assaying, all frogs are discarded which contain an excess of fluid in the lymph sac one hour after being injected, quite uniform and reliable results are obtained by the one-hour frog-heart method.

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STILLINGIA SYLVATICA.

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The root of *Stillingia sylvatica* has been a popular remedy in the Southern States for more than a century. It was first introduced to the medical profession by Thomas Young Simons, in an article published in 1828, in the American Medical Recorder.

In 1846, Dr. H. B. Frost[1] published a paper on Stillingia in which he considered it "not very far inferior to mercury in its action upon the capillary and secreting vessels in changing their morbid states or conditions."

In 1850, the root of *Stillingia sylvatica* was introduced into the United States Pharmacopœia and has occupied the position of an official remedy ever since.

Concerning the value of the drug there is very great divergence of opinion, but it is still largely used in domestic practice, chiefly as an alterative, and by the medical profession, especially in the form of certain proprietary remedies of which it forms an ingredient. Notwithstanding its long use, however, there is very little known concerning the chemistry of the plant, the pronounced acridity of the drug being attributed to a volatile oil, a fixed oil and a resin called sylvacrol.

The Volatile Oil:—The term "oil of stillingia" has been applied to two products of very different character, meaning on the one hand a preparation obtained from the root by steam-distillation and on the other an alcoholic or ethereal extract of the same. To add to this confusion there are contradictory reports concerning the presence of volatile oil in the root. Thus, W. Saunders[2] extracted five pounds

1. Am. Jour. Pharm., 20, 306.
2. Proc. A. Ph. A., 1868, 460; Am. Jour. Pharm., 41 (1869) 149.