

ever, I have found that the home merchants sometimes feel that they are indispensable and are very indifferent about service; they are repeatedly out of some merchandise that is needed without delay. I have spent some anxious days worrying over depleted stock that the jobber could not replace.

In many hospitals pharmacists do not have the privilege of even buying the drugs. In my opinion this is a great mistake, for no one is better informed regarding them, if qualified, than the pharmacist. I do not see how he can keep posted on prices if he is not buying. Nor can he keep interested in his profession if he is only acting as a "mechanical mixer" of drugs. I know a private hospital where the pharmacist makes her requisitions to one who acts as official buyer for the entire hospital. Her requests are sometimes overlooked, and again his purchases are made to accommodate certain individual salesmen or concerns rather than to save money for the institution. A pharmacist working under such conditions is indeed handicapped. I surely cannot conceive how any individual can be so versatile as to be able to buy intelligently and wisely for every department in the hospital from the attic to the basement. I think buying for the hospital pharmacy should be left to the pharmacist alone.

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RESEARCH NOTES ON STABILITY OF ELIXIR LACTATED PEPSIN,  
SOLUBILITY OF CHLOROFORM IN SIMPLE SYRUP, U. S. P. OINTMENT  
OF ZINC OXIDE WITH PETROLATUM BASE, AND FLUIDEXTRACT OF  
GLYCYRRHIZA—SUGGESTION FOR AN IMPROVED FORMULA.\*

BY FREDERICK J. AUSTIN.

STABILITY OF ELIXIR LACTATED PEPSIN.

A ruling by the Prohibition Commissioner, issued early in June 1920, placed those alcohol-containing liquid pepsin preparations, which contained less than 8 grains of standard pepsin U. S. P. per fluidounce, in the beverage class. As a result manufacturers faced the alternative of discontinuing many of these products or of making a decided increase in their pepsin strength.

A manufacturer generally does, and should always, possess reliable data regarding the keeping qualities of his products. This is particularly necessary with the liquid preparations of animal enzymes. On account of the decided increase necessary in the pepsin content of many Elixirs of Lactated Pepsin, if they were to be marketed at all, experiments were undertaken with the idea of determining the stability of these altered preparations under ordinary storage conditions.

In view of the specific nature of the new requirement and of the unavoidable slight variations in assay results due to the personal equation, it was decided that such preparations could not be manufactured and sold with safety if they contained exactly 8 grains of enzyme per fluidounce, but that they should represent at least 10% above the required label claim of 8 grains per fluidounce.

Accordingly, two one-gallon samples were set aside, the first of which represented a lot of the elixir in question containing 8.8 grains of official pepsin per fluidounce. An alcohol determination on this sample showed the presence of 11.72% absolute alcohol by volume, the label claim being 12%. A second gallon sample was pre-

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\* Scientific Section, A. Ph. A., Cleveland meeting, 1922.

pared, containing 7.4 grains of official pepsin per fluidounce and sufficient pancreatin U. S. P. and diastase U. S. P. to make a total enzyme content of 8.8 grains per fluidounce. This elixir contained 14.92% absolute alcohol by volume, being intended to contain 15%.

At the outset both elixirs when assayed by the official method for pepsin showed the proper pepsin strength, all but a trace of the coagulated egg albumen being digested in each of the duplicate trials. Thereafter each sample was treated as a routine job, both having been made from materials regarding the strength of which the Ferments Manufacturers made a definite claim which claim was confirmed when the products were purchased. The presence of enzymes other than pepsin in the second sample was ignored. It should also be noted that above samples exhibited the usual pleasant flavor and odor which one associates with these elixirs.

These assays and examinations as regards physical condition were repeated monthly, the period of observation dating from July 15, 1920. The results were satisfactory for one year, there being during that period no marked increase in the amounts of undigested egg albumen nor any perceptible deterioration as regards flavor or odor. On the fourteenth trial, that of August 15, 1921, however, the pepsin assays were failures, between two and three cubic centimeters of coagulated egg albumen remaining undigested. The odor of each preparation was offensive and the taste nauseating.

The indications are, therefore, that, under the conditions prevailing, Elixir Lactated Pepsin made with 8.8 grains of digestive ferment to the fluidounce (pepsin alone or pepsin combined with small quantities of pancreatin U. S. P. and diastase U. S. P.) should not be dispensed if more than one year old.

#### SOLUBILITY OF CHLOROFORM IN SIMPLE SYRUP U. S. P.

Pharmaceutical manufacturers frequently prepare various non-alcoholic syrups having essentially the density of U. S. P. Simple Syrup which are claimed to contain a specific amount of chloroform per fluidounce. These claims, at times, seem ridiculously high, particularly when they call for four or more minims per fluidounce. Syrup White Pine Compound with Chloroform may be mentioned as a typical example of the class of syrups referred to.

According to the ninth revision of the U. S. Pharmacopœia one part of chloroform is soluble in 210 parts of water. Slightly less than 2.3 minims, therefore, should be soluble in 1 fluidounce (480 minims) of this solvent.

On the surface at least this official statement alone controverts claims calling for the presence of three or more minims of chloroform in solution in the specified quantity of non-alcoholic syrups. The question may be raised as to whether the presence of the sugar increases its solubility.

With the idea of investigating this problem, seven graduated cylinders of practically the same capacity and having perfectly fitted stoppers were three-quarters filled with Simple Syrup, having a specific gravity of 1.31 at 25° C. These were numbered from one to seven and to the first was added one minim of chloroform to the fluidounce, to the second, one and one-half minims per fluidounce, etc., by half-minim steps to 4 minims of chloroform per fluidounce in cylinder number seven. These were frequently and vigorously shaken for one week. The chloroform in numbers one and two containing, respectively, one minim and one and one-

half minim per fluidounce promptly dissolved and that in number three, which contained two minims per fluidounce, eventually disappeared completely. Varying amounts of chloroform dependent, of course, on the quantities added remained undissolved at the end of the period of agitation in the remaining cylinders. After standing for forty-eight hours, to allow for complete separation of undissolved chloroform, ten cubic centimeter duplicate samples (*a*) and (*b*) were drawn from each cylinder for assay, the dissolved chloroform being separated by distillation with alcohol, decomposed under pressure with alcoholic potassium hydroxide and the resulting potassium chloride titrated with tenth-normal silver nitrate V. S., a blank determination being run for the amount of alcoholic potassium hydroxide used in each assay and results corrected accordingly.

TABULATION OF RESULTS OF ASSAY.

No. of cylinder.	Minims CHCl <sub>3</sub> per fluidounce.	N/10 AgNO <sub>3</sub> V. S. Consumed by 10 cc samples.	Minims CHCl <sub>3</sub> found per fluidounce.
1	1	(a) 7.43 cc	0.96
		(b) 7.90 cc	1.02
2	1.5	(a) 11.52 cc	1.49
		(b) 11.20 cc	1.45
3	2	(a) 14.25 cc	1.84
		(b) 13.63 cc	1.76
4	2.5	(a) 13.55 cc	1.75
		(b) 14.25 cc	1.84
5	3	(a) 13.94 cc	1.80
		(b) 14.40 cc	1.86
6	3.5	(a) 13.32 cc	1.72
		(b) 13.86 cc	1.79
7	4	(a) 13.48 cc	1.74
		(b) 13.32 cc	1.72

Calculations were based on the following: Weight of 1 minim of chloroform—0.0911 Gm.—1 cc of N/10 AgNO<sub>3</sub> V. S. equals 0.0039796 Gm. of chloroform.

The average solubility shown in those determinations to which 2 or more minims of chloroform per fluidounce had been added was 1.78 minims.

Trials of a similar nature were made on request by another chemist who attempted to dissolve one, two, three, five, six and ten minims of chloroform in one fluidounce of Simple Syrup U. S. P. He found that two minims or less dissolved in such syrup without leaving a perceptible trace of undissolved chloroform. His assays of those specimens to which he had added between two and ten minims chloroform per fluidounce showed amounts ranging from 1.60 to 1.79 minims chloroform per fluidounce.

It would appear therefore that the presence of sugar in solution does not increase, but rather retards the solubility of chloroform in Simple Syrup and we are forced to conclude that claims of the presence of more than two minims per fluidounce in non-alcoholic syrups of the above-mentioned density are erroneous and that its addition is not only useless but wasteful.

#### OINTMENT OF ZINC OXIDE WITH PETROLATUM BASE.

For the manufacture of Ointment Zinc Oxide, the Pharmacopœia directs that the zinc oxide be rubbed with about one-fourth of the required amount of melted benzoinated lard in a warmed container, that the remainder of the ben-

zoinated lard, previously melted, be incorporated with this mixture and the whole thoroughly stirred until it congeals.

According to the same authority, the melting point of lard may range from 36° to 42° C. It contains no specification as regards the melting point of benzoinated lard, but market products of this item usually melt between 36° and 37° C.

Ointment of Zinc Oxide made with benzoinated lard frequently becomes so soft in hot weather that it is in no condition for shipment and at times a considerable separation of zinc oxide takes place. Also the ointment is prone to take on a granular condition and, in spite of the fact that the lard is benzoinated, it often becomes quite rancid.

Experimental lots of the ointment were made in which the benzoinated lard was replaced with the so-called Lily White and Snow White petrolatums of the market, which melted at from 41 to 42° C. (the upper limit for lard). The color of these petrolatums varied from pale yellowish white to pale greenish white. The resulting ointments were of good color and did not become rancid or granular, but they showed evidence of separation when heated over night at 107° F. (41<sup>2</sup>/<sub>3</sub>° C.). Specimens were then made of the proper oxide strength containing 5%, 10% and 15% of paraffin, respectively, with the result that the first showed separation on heating to the above-mentioned temperature, and whereas the last two did not, they became so firm on cooling to a temperature of 60° F. for six hours that they would not flow from collapsible tubes under ordinary pressure.

The problem narrowed down to the finding of a white petrolatum with a higher melting point, one which did not become too firm when reasonably cool. Such a product has been found to be available with a practically constant melting point (47° to 48° C.) and almost without color. It yields a white ointment which stands prolonged heating not only to 107° F., but to 110° F., without separation and which may also be cooled to 60° F. without becoming unduly firm.

#### FLUIDEXTRACT OF GLYCYRRHIZA.

*(Suggestion for an Improved Formula.)*

For the manufacture of this Fluidextract, the U. S. P. directs that 300 cc of 10% ammonia water be mixed with 2700 cc of chloroform water and that 1000 Gm. of glycyrrhiza, No. 20 powder, be moistened with this menstruum. The drug is then packed in a percolator, saturated with the above liquid, macerated for 48 hours and percolation then carried to exhaustion, reserving the first 500 cc of percolate and evaporating the remainder to a soft extract. This soft extract we are directed to dissolve in the reserve, adding if necessary a few drops of ammonia water as an aid to solution. Alcohol, 250 cc, is then added, the fluid put aside for 7 days, the clear liquid decanted, the remainder being filtered and the filter washed with a mixture of one volume of alcohol and three volumes of water sufficient to yield 1000 cc.

The concentration of the weak percolate obtained above yields a very acid, difficultly soluble soft extract. When mixed with the reserve, which by the way contains a small amount of chloroform which is not removed, is diluted to 750 cc with water and brought to volume with alcohol, this soft extract is responsible for the excessive sedimentation which occurs during the specified period. The prep-

aration often becomes almost gelatinous, efficient filtration is impossible, and the average yield on a manufacturing scale is 25% of the theory.

Various experimental lots were made in accordance with specifications with like results. Trials were then made using in turn, as extracting menstruums, cold water, chloroform water, water at 40° C., at 60° C., at 80° C., at 90° C., and finally boiling water, eliminating the ammonia water entirely. Chloroform water, aside from its preservative action, showed no advantage over distilled water at the same temperature. As the temperature of the extracting menstruum was raised, there was noticeable a marked decrease in the amount of the albuminous material present and filtration at the end of the process was observed to be increasingly rapid. With boiling water this substance gave practically no trouble.

Several large batches of this fluidextract have been made without difficulty and, after the lapse of more than a year, the condition, flavor and odor of the record samples are entirely satisfactory.

The working formula is as follows:

#### FLUIDEXTRACT OF GLYCYRRHIZA.

Glycyrrhiza No. 20 powder .....	1000 Gm.
Alcohol .....	250 cc
Boiling Water q. s.	
Cold Water q. s.	

Moisten 1000 Gm. of Glycyrrhiza with sufficient boiling water, pack in percolator, cover with boiling water and macerate, keeping hot over night. Percolate to exhaustion with boiling water, reserving first 500 cc collected. Evaporate weak liquor to a soft extract, dissolve in reserve and, if necessary, make up to 750 cc with water. Gradually add 250 cc of alcohol with constant stirring, let stand one week, siphon off clear fluid and filter remainder, wash residue on filter with q. s. of a mixture of one volume of alcohol and 3 volumes of water to make 1000 cc.

Precautions must, of course, be taken during warm weather to keep the reserve percolate sweet.

This formula has been submitted to the U. S. P. Revision Committee with the recommendation that it receive consideration.

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#### VOLUME PRODUCTION PHARMACY.\*

BY WILLIAM H. GESELL.

The phrase, *Volume Production Pharmacy*, applied in this way, may be new to you, and it is really an entirely different type of pharmacy than you and I were taught in college.

*Volume Production Pharmacy* is the result of the present trend of pharmacy. Formerly, when a person went into a drug store and purchased pharmaceutical preparations, he patronized that drug store because he knew the proprietor, knew of his training, knew that his preparations were made by him in a careful, scientific and honest manner—he depended on his honesty for their reliability. Perhaps this condition would have continued indefinitely as it has in other countries where there are laws that the pharmacist must be the individual owner. But in the

\* Parts of an address before New York Branch, A. Ph. A.