

Shake frequently during 12 hours, allow to separate, and decant 160 mls (representing 4 Gm. of cinchona). Extract the alkaloids from this by successive shakings with weak sulphuric acid, mix the acid solutions, add an excess of ammonia and extract with successive portions of chloroform. Evaporate (or distil) off the chloroform, add 5 mls of alcohol to the residue, again evaporate, dry at 100° C. and weigh.

SUMMARY.

Hydrochloric acid not only facilitates the extraction of alkaloids from cinchona red as well as yellow, but it also stabilizes the preparations by reducing precipitation. Acid should be used in at least sufficient amount to convert the alkaloids present into normal hydrochlorides. The use of this acid is, therefore, recommended for tincture of cinchona and compound tincture of cinchona, as well as for all fluidextracts and extracts of cinchona. The influence of acid in promoting stability is shown more clearly in another paper.

In the assay of cinchona a preliminary treatment of the drug with hydrochloric acid results in a purer alkaloidal residue for either weighing or titration, hence is more accurate. The results, while less than by the present official process, are more nearly correct. The process is also improved by changing the proportions of ether-chloroform from 2 to 1 to 3 to 1.

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THE FUNCTION OF GLYCERIN IN TINCTURES AND FLUID-EXTRACTS.*

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A considerable number of our fluidextracts and tinctures contain a small proportion of glycerin, usually ten percent by volume, which is employed to prevent or reduce precipitation. That it often is efficacious in this respect is beyond doubt. There is also a marked tendency toward an increased use of glycerin for this purpose, and in nearly all cases the glycerin is employed as a solvent, being a part of the menstruum used in extracting the drug.

It has also been observed that, other things being equal, percolation is not as rapid when glycerin comprises a part of the menstruum as when it is absent, and furthermore it is thought that drugs do not exhaust as rapidly when a glycerinated menstruum is employed as when alcohol-water only is used. This latter impression may come from the slower flow of the glycerinated percolate, or it may be that glycerin is not as good a solvent as has been thought.

The question how glycerin acts in preventing precipitation seems never to have been investigated. Does glycerin act through its solvent power? Or does it prevent precipitation by hindering oxidation or other chemical changes in the drug extracts? Or is the added viscosity an important factor? Is it most effective when used in the menstruum or when added to the (over-strength) percolate? These questions are worth investigating. In this paper the investigation has been confined to preparations official in the U. S. Pharmacopoeia and the National Formulary.

*Read before Scientific Section, A. Ph. A., City of Washington meeting, 1920.

The method adopted has been to extract two different portions of the same lot of drugs, under as nearly equal conditions as possible, using the official glycerinated menstruum on one portion and an alcoholic menstruum of the same alcoholic strength on the other. Care was taken to have the temperatures, rates of flow and size and form of percolates equal or, when different quantities were percolated, relative. Thus, when 250 Gm. of drug was percolated with a glycerinated menstruum and 750 or 1000 Gm. with the alcoholic menstruum, the required amounts of percolates were obtained in the same time, or as nearly as possible. The rate and conditions of exhaustion were, therefore, the same.

The preparations made with glycerinated menstrua were finished in the usual way. Those made without glycerin were adjusted to strength by means of the menstruum, and also by addition of glycerin in the same amounts as used in official preparations, by addition of sugar and menstruum, and by addition of glucose and menstruum. The corresponding preparations were all finished on the same day, were compared for color and strength, and were then set aside to observe their keeping qualities. In adding sugar or glucose to different samples we get some information regarding the action of chemical retardance and also of added viscosity in preventing precipitation.

In many instances the percolates for making fluidextracts were collected in fractions, the first being 80 mils for 100 Gm. of drug, the second, third, fourth and fifth being 100 mils each. These were examined separately to learn the rate of extraction.

ALKALOIDAL DRUGS.

The only official alkaloidal preparations containing glycerin are the fluidextracts of cinchona and hydrastis, and the tinctures of cinchona. This study was coupled with a study of the influence of hydrochloric acid on cinchona (reported in another paper), and the percolations were made to serve a double purpose.

Cinchona.—Both calisaya and red cinchona were tried. Unfortunately, in the list of 48 different preparations made, the relative rates of exhaustion of cinchona with and without glycerin were overlooked. But the results on the tinctures indicate clearly the influence of glycerin on this drug.

Tincture of calisaya made with two-thirds alcohol assayed 1.11 Gm. of alkaloids per 100 (from a 7.1% drug), showing 70.5% of exhaustion. A corresponding tincture made with the official glycerinated menstruum assayed 1.02 Gm. of alkaloid per 100, showing 66.1% of exhaustion.

When hydrochloric acid was used in the menstruum the resulting tinctures assayed, (a) with glycerin 1.2 Gm. per 100 or 78.1% exhaustion, (a) without glycerin, 1.37 Gm. per 100 or 87% exhaustion; (b) with glycerin acidulated, 1.42 Gm. per 100 or 90% exhaustion; (b) without glycerin acidulated, 1.45 Gm. per 100 or 92% exhaustion. More acid was used in (b) than in (a).

Compound tincture of cinchona, made from a red cinchona assaying 10.55% of alkaloids, showed:

With glycerin 1.0 Gm. per 100 or 85.8% exhaustion.

Without glycerin 0.975 Gm. per 100 or 74.6% exhaustion.

With glycerin, acidulated, 1.02 Gm. per 100 or 87% exhaustion.

Without glycerin, acidulated, 0.935 Gm. per 100 or 80% exhaustion.

Here we find a retarding effect of glycerin in extracting calisaya and an accelerating effect on red cinchona.

Fluidextracts of both drugs were adjusted to contain 4.5 Gm. of alkaloids per 100 mils, and also to contain (a) no acid; (b) 1% of acid (hydrochloric) and (c) 2.5% of acid in red cinchona.

Samples of each also were adjusted to contain no glycerin, 10% of glycerin, 10% of granulated sugar and 10% of glucose. These have all been kept 18 to 21 months in 8 oz. amber bottles in a moderate light and an equable temperature.

The stability of these preparations is shown as follows:

TABLE SHOWING PRECIPITATION IN CINCHONA PREPARATIONS.

Preparation.	No glycerin.	Glycerin.	Sugar.	Glucose.
<i>Calisaya Fluidextract</i>				
Neutral menstruum.....	marked	slight trace	trace	slight
Acid menstruum.....	considerable	slight trace	slight trace	slight
<i>Calisaya Tincture</i>				
Neutral menstruum.....	considerable	(a) none (b) very slight trace	very slight trace
Acid menstruum....(a)..	none	none	none	none
Acid menstruum....(b)..	none	none	none	none
<i>Red: Fluidextract</i>				
Neutral menstruum.....	considerable	very slight trace	very slight trace	considerable
Acid menstruum....(c)..	considerable	marked	marked	marked
<i>Compound Tincture</i>				
Neutral menstruum.....	considerable	(a) slight slight	considerable	considerable
Acid menstruum.....	(b) marked	(a) slight (b) slight	marked	marked
Acid menstruum.....	(c) slight trace	none	slight trace	slight trace

("a" indicates the preparation made with glycerinated menstruum, and (b) when glycerin was added to the percolate.)

With both cinchonas, acid is shown to be more efficient than glycerin in preventing precipitation but glycerin also shows a marked action. The results are the same whether the glycerin is used in the menstruum or is added to the percolate.

In the preparation of calisaya, sugar and glucose appear to be equal to glycerin in preventing precipitation, but not in those of red cinchona. In the latter sugar and glucose show no influence.

A further influence of glycerin in compound tincture of cinchona was seen, in that while 7.5% of glycerin reduced the precipitation from considerable to slight, 15% (in an extra test) almost entirely inhibited change. Furthermore, in reducing the percolate from 0.93 Gm. of alkaloids per 100 to 0.45 Gm. per 100, when the dilution was made with 64% alcohol, as directed in the Pharmacopoeia, considerable precipitate appears on standing, both on the bottom and sides of the bottles, while when diluted with the 64% alcoholic menstruum containing 7.5% of glycerin no precipitation has appeared in 18 months. Here is a suggestion that in diluting this tincture and the fluidextracts to standard strength, the proportions of glycerin as well as of alcohol should be maintained.

With regard to the greater influence of glycerin on red cinchona than on calisaya, both in facilitating extraction and in preventing precipitation, it is to be remembered that red cinchona is much richer in tannoid bodies and that glycerin is a particularly good solvent for these.

Hydrastis.—A drug assaying 2.98% of ether-soluble alkaloids was used. From this two fluidextracts were made, one with glycerinated (official) menstruum and one without glycerin. The several fractions of percolate were assayed, resulting as follows:

	Glycerinated menstruum.		No glycerin.	
	% alkaloid.	% exhaustion.	% alkaloid.	% exhaustion.
First fraction.....	2.52	67.5	2.86	76.78
Second fraction.....	0.72	24.16	0.55	18.45
Third fraction.....	0.094	3.15	0.03	1.00
Fourth fraction.....	0.02	0.67	0.009	0.38
Total.....		85.48		96.61

Here the glycerin shows a marked retarding effect on extraction.

Fluidextracts were then finished from each percolate, adjusted to 2% of ether-soluble alkaloids and the non-glycerinated percolate was divided into four portions and made to contain no glycerin, 10% of glycerin, 10% of sugar and 10% of glucose, respectively; adjusted to alkaloidal and alcoholic strength and set aside.

The percolate from the glycerinated menstruum was also divided, one portion being diluted to standard with 64% alcohol (as directed in the Pharmacopoeia), the other with 64% alcohol containing 10% of glycerin. After 17 months the precipitation in the sample which was diluted with glycerinated menstruum shows approximately the same amount of sediment as that diluted with hydro-alcohol, precipitation being slight in each case. The sample without glycerin contains the most sediment of all but even this is not heavy. The sample to which glycerin was added corresponds to the U. S. P. sample, and those containing sugar and glucose contain slightly more.

In this case both sugar and glucose have hindered precipitation but not quite as effectively as glycerin. The addition of glycerin to the percolate is preferable in this case because extraction is more rapid without it, and the influence on stability is just as good.

CATHARTIC DRUGS.

The two cathartic drugs whose preparations contain glycerin are rhubarb and juglans. In both of these the active principles are anthraquinone bodies, which give an intense red color with alkalis, and this reaction was used as a basis for estimating the relative extraction and activity of the preparations.

To 100 mils of distilled water, contained in a nesslerizing tube, was added 5 mils of stronger water of ammonia, then sufficient of the preparation to produce a pronounced reddish tint when viewed lengthwise through the tube, sufficient of each preparation being used to produce the same tint or depth of color. This gives the relative strength of two preparations of the same kind. Rhubarb was not compared with butternut, but only rhubarb with rhubarb, aromatic tincture with aromatic tincture, sweet tincture with sweet tincture, etc. Since the volume of water and its alkalinity are the same in each test, this should indicate the relative activity of the preparations tested, though it gives no indication of their absolute value.

The tints did not match in all cases, since glycerin, when used as a menstruum, extracts more of the coloring matters from most drugs than does alcohol-water, and this influences the tint obtained. Hence the figures are approximate only, and are useful as showing differences to an approximate extent. The fluidextracts of these drugs will show a very distinct red tint with alkali in dilutions of 1 in 50,000.

Rhubarb.—The percolates for fluidextract were received in fractions and tested separately. The figures which follow show the dilutions at which the red tints matched, and are good for each pair only. They are not interchangeable since no effort was made to match to a standard tint.

<i>Fluidextract Rhubarb U. S. P.</i>	1st	2nd	3rd	4th
Glycerinated menstruum.....	1 : 40000	1 : 10000	1 : 1000	1 : 700
No glycerin.....	1 : 50000	1 : 6000	1 : 2000	1 : 1000

This shows a marked retardation of extraction by glycerin. The glycerinated percolates were deeper in color, as received, but showed a less rapid exhaustion of the drug. The finished fluidextracts tested equal in cathartic activity (1 : 50,000 each) as nearly as could be judged but the glycerinated menstruum extracts so much more of the yellow color that it was difficult to judge the red tint produced by the alkali.

In specific gravity, the U. S. P. sample was 1.0625 and the sample to which glycerin was added, 1.0325. This indicates a difference in extractive matters in favor of the glycerinated menstruum. The medicinal value of rhubarb is due not only to its cathartic but also to its astringent principles, and it is probable that these are better extracted by the glycerinated menstruum.

In stability there is little choice between the five samples, after standing eighteen months. All have precipitated badly—there being about 3 millimeters of sediment in each 250-mil bottle but the sample without glycerin shows no greater precipitate than those with glycerin or with

sugar or with glucose. None of these protectives show any marked advantage in this preparation.

Tincture of Rhubarb, U. S. P.—This was made entire, and tests on the finished preparations show the U. S. P. tincture to be about one-tenth weaker than that made without glycerin. The specific gravities correspond to that of the U. S. P. tincture, being 0.9947, while that in which glycerin was added to the percolate is 1.0065.

In stability there is again little choice. All have precipitated badly—about 2.5 millimeters covering the bottoms of 250-mil bottles—and the sample containing no glycerin appears to be no worse than the others. Possibly there is a little less precipitate in the sample containing 20% of sugar than in the others, but the difference, if any, is small and may be ascribable to a slightly greater density in the precipitate.

Aromatic Tincture of Rhubarb, U. S. P.—This corresponds in a measure with the plain tincture, but the differences are not as great. The tincture made with glycerinated menstruum is about one-twentieth weaker than that without glycerin. The specific gravities are 1.0005 and 1.0075, respectively—in this case the official tincture being lighter.

In stability there is little choice. These samples have not precipitated nearly as heavily as the plain tinctures, and slight differences are more noticeable. The sample containing no glycerin appears the best, and there is no choice between the official tincture and the one in which glycerin was added to the percolate. Sugar (20%) seems to have reduced precipitation slightly and glucose to have increased it. But the differences are all too small to draw conclusions from, and are not marked in any case.

Sweet Tincture of Rhubarb, N. F.—Here again the N. F. (glycerinated menstruum) tincture tests about one-tenth weaker than the non-glycerinated. The specific gravities are 0.9823 and 0.9920, respectively—again a trifle lighter in the official tincture.

In stability there is also no choice, each 250-mil bottle showing about 4 millimeters of precipitate at the bottom.

For rhubarb the above series shows a distinct disadvantage in the use of glycerin in the menstruum where it decreased the solvent action and hinders extraction. But it shows no advantage in preventing precipitation, at least in the proportion in which it is used.

It should be noted that in the above tinctures the proportions of sugar and glucose used was 20 Gm. per 100, or double that which would correspond to the glycerin. This practically saturates the fluidextract (in which less than 10 Gm. per 100 dissolved) and probably nearly saturates the tinctures, but no advantage is seen in their use.

Butternut.—The fluidextract was percolated in fractions, and the different fractions tested as follows:

	1st.	2nd.	3rd.	4th.
Glycerinated menstruum	1 : 55,000	1 : 2000	1 : 800	1 : 450
No glycerin	1 : 50,000	1 : 2000	1 : 1000	1 : 500

This shows a slightly more rapid extraction with the glycerinated menstruum, but the difference is small. The fluidextracts are equal in value. The N. F. fluidextract has a specific gravity of 1.0725 and the other 1.0720.

It was very difficult to judge the relative stability of these samples. The fluid is so black and thick that in an amber bottle a considerable precipitate is not easily seen. Precipitation in liberal quantities had occurred in all samples, the precipitate adhering to the sides as well as the bottom of the bottles. By carefully pouring out the liquid and examining the precipitate close to an electric light the one containing 10% of sugar showed less precipitation than any of the others. In the rest the precipitates appeared to be about equal in amounts.

ASTRINGENT DRUGS.

Since glycerin is, without question, a good solvent for tannin, it is not surprising that most of the liquid preparations of the astringent drugs are made by use of glycerin in the menstruum. Hence this class is the largest in the present series.

For the estimation of relative strength and exhaustion the method of S. T. Hinsdale was adopted as being the simplest and easiest of many methods published.

It is adaptable to all the various kinds of tannin, though many methods, some of them more reliable for specific tannins, are not.

The method is given in Allen's Organic Chemistry, 4th edition, Vol. V, p. 94, and consists in comparing the colors produced with ferric chloride, using a standard solution of tannin. The reagent, which was made fresh each time since it does not keep well, consists of a solution of 0.04 Gm. of potassium ferrocyanide and 1.5 mls of solution of ferric chloride in sufficient water to make 500 milliliters; 5 mls of this reagent is mixed with 95 mls of distilled water in a colorimetric tube, then the astringent preparation—or usually a dilution of it—is added in sufficient quantity to match the color produced by adding 0.1 mil of a 0.1% solution of pure tannic acid to a corresponding dilution of the reagent in another colorimetric tube. This amount of tannic acid is enough to give a distinct, even a fairly deep blue-black color when viewed lengthwise through the tube.

Since the object sought was not an accurate estimation of the tannin, but the relative strength of two preparations of like character, the tannic acid solution was not used as a standard but was employed as a guide in determining the depth of color best suited for comparison. The estimations, therefore, were purely comparative, the whole effort being directed to ascertaining the relative amounts of the astringent preparations (of the same kind) required to produce the same degree of color.

Geranium.—The N. F. fluidextract was made and the percolates collected in fractions. Following are the colorimetric estimations:

	1st. fraction.	2nd. fraction.	3rd. fraction.	Fluidextract.
Glycerinated menstruum.....	1 : 33000	1 : 25000	1 : 5000	1 : 50000
No glycerin.....	1 : 50000	1 : 20000	1 : 1600	1 : 50000

The finished fluidextracts, each containing glycerin (one in the menstruum and the other added to concentrated percolate) had a specific gravity of 1.0775 and 1.0755, respectively.

In this case glycerin retarded extraction, but the finished preparations were of equal value.

The sample containing no glycerin has precipitated more than those with glycerin, and those containing sugar and glucose are a little heavier in precipitation than those which contain glycerin. In other words, both sugar and glucose have reduced precipitation but not as much as glycerin, and in the latter case the glycerin added to the percolate shows slightly less precipitate than the glycerinated menstruum preparation.

Hamamelis.—The fractions obtained in making the fluidextract tested as follows:

	1st. fraction.	2nd. fraction.	3rd. fraction.	Fluidextract.
Glycerinated menstruum.....	1 : 50000	1 : 10000	1 : 200	1 : 50000
No glycerin.....	1 : 25000	1 : 6250	1 : 150	1 : 42000

Here we find a very decided advantage in the use of glycerin, the first fraction (80% of drug) being twice as strong as that without glycerin, and the finished fluidextract also showing marked difference in strength. The N. F. fluidextract has a specific gravity of 1.094 and the one to which glycerin was added is 1.0895, indicating a difference in the amount of extractive.

The sample made without glycerin contained, after standing 16 months, about 12 millimeters of gelatinous, caked precipitate. The one made with glycerinated menstruum contains about 5 millimeters of a light brown, fine precipitate, and the ones to which glycerin or sugar was added contain about 3 millimeters of the same kind of precipitate. Glucose also appears to have inhibited precipitation, but the precipitate here is sticky and darker in color.

Krameria.—The fractions obtained in making the fluidextract tested as follows:

	1st. fraction.	2nd. fraction.	3rd. fraction.	Fluidextract.
Glycerinated menstruum.....	1 : 50000	1 : 1666	1 : 500	1 : 50000
No glycerin.....	1 : 20000	1 : 500	1 : 500	1 : 40000

Again a marked advantage for glycerin in the menstruum, extraction being more than twice as rapid and the finished preparation much stronger. The specific gravities did not show so much variation, being 1.059 and 1.060, respectively.

The two samples containing glycerin have deposited, in 16 months, a thin coating of precipitate on the bottoms of the bottles, that containing sugar a little thinner coating, and the one containing no glycerin about three times as much. Glucose also has hindered precipitation but not as much as the others. It may be noted again that *Krameria* preparations do not precipitate badly but the tannin hydrolyzed easily and the astringency may have been lost in a preparation which remains nearly or quite clear.

Nutgall.—Two tinctures were made, with and without glycerin, respectively. The one containing glycerin tested 1 : 80000 and the other 1 : 56000. Again a marked advantage in the use of glycerin.

The sample containing glycerin shows no precipitate after 15 months, while the other has a coating of insoluble matter about 1 millimeter thick on the bottom of the bottle.

Quercus.—The fractions obtained in making the fluidextract tested as follows:

	1st. fraction.	2nd. fraction.	3rd. fraction.	Fluidextract.
Glycerinated menstruum.....	1 : 33000	1 : 1000	1 : 500	1 : 50000
No glycerin.....	1 : 50000	1 : 1000	1 : 500	1 : 50000

This shows a retarding action of glycerin in extracting the drug, but the fluidextracts are equal. The specific gravities are 1.0360 and 1.0335, respectively.

Precipitation is very slight in all cases, the one in which glycerin was added in the final adjustment showing none. The others show only a slight deposit on the bottom of the bottles. Sugar again shows an inhibiting effect but not equal to glycerin.

Rhus Glabra.—The fractions obtained in making fluidextracts tested as follows:

	1st. fraction.	2nd. fraction.	3rd. fraction.	Fluidextract.
Glycerinated menstruum.....	1 : 40000	1 : 10000	1 : 500	1 : 50000
No glycerin.....	1 : 50000	1 : 5000	1 : 166	1 : 50000

Here glycerin shows a retarding effect on the extraction of the drug, but the fluidextracts are equal. The specific gravities are 1.043 and 1.045, respectively.

All of the samples show a deposit about 1 millimeter thick of a light brown diffusible precipitate which is about the same in amount in all cases. Neither glycerin, sugar nor glucose shows any marked influence on precipitation in this case.

Rose.—The fractions tested as follows:

	1st. fraction.	2nd. fraction.	3rd. fraction.	Fluidextract.
Glycerinated menstruum.....	1 : 66000	1 : 25000	1 : 1000	1 : 65000
No glycerin.....	1 : 50000	1 : 12500	1 : 2000	1 : 50000

Glycerin again shows a decided advantage as a menstruum. The specific gravity of the U. S. P. preparations is 1.1565 while that containing the added glycerin is 1.1705. Apparently glycerin used as a menstruum does not add to the extractive matter in the fluidextract, though it increases the tannin.

The U. S. P. sample has deposited a thick magma in 17 months, while that containing no glycerin shows only about a quarter as much, and those to which glycerin and sugar were added, about one-eighth as much. This is an anomalous condition, but apparently sugar is nearly as effective a preservative as glycerin in this preparation.

MISCELLANEOUS.

There remain ten preparations containing glycerin, the greater portion of which owe their chief value to their flavoring qualities.

None of these contain active principles which can be estimated chemically. The only way of comparing them is by their general appearance, color and taste. The taste was compared in very dilute solutions, adjusted to be near to the limit of extension, so that any very marked differences in strength or quality of flavor

would be noticeable. Sweetened water was used as the diluent, the quantity of sugar being used equal in each pair employed for comparison. In these dilutions comparatively small differences become noticeable, and the coloring properties are also comparable, so that while the comparisons are purely physical, the results are fairly satisfactory, particularly on preparations which are employed chiefly for their physical effects.

Apocynum.—The N. F. fluidextract was made with and without glycerin. The first fractions only were compared, that made with glycerinated menstruum having a distinct bitter taste in dilution of 1 : 2500 while that without glycerin had a corresponding bitterness in dilution of 1 : 2000. The latter was also lighter in color.

Precipitation is slight in all cases. The sample containing sugar is almost clear, while those containing glycerin and glucose show a distinct trace. The sample without glycerin is fully as good in this respect as are those with glycerin.

Cardamom-Compound, Tincture of.—Tinctures made with and without glycerin were indistinguishable in taste in dilutions of 1 : 1000. In color and general appearance they are alike. The specific gravities (glycerin being added to the second) are 0.9530 and 0.9526, respectively.

None of the samples have precipitated perceptibly except the one to which glucose was added. This shows a trace of sediment on the bottom.

Cinnamon.—Two tinctures, one made with and one without glycerin, show no difference in taste when diluted 1 : 500. They are also alike in odor, but the U. S. P. tincture (made with glycerinated menstruum) is a deeper red than the other. This is in accordance with the usual superiority of glycerin in extracting coloring matters from the drugs. It is particularly noticeable in this preparation. The specific gravities are 0.905 and 0.9315.

All of the samples show just a trace of precipitation after standing a year, there being no choice in this regard except that the one containing glucose is a trifle the heavier—or perhaps the more sticky and noticeable.

Columbo.—The fluidextract was made and the fractions compared in taste in the following dilutions:

	1st. fraction.	2nd. fraction.	3rd. fraction.	Fluidextract.
Glycerinated menstruum.....	1 : 4000	1 : 500	1 : 250	1 : 5000
No glycerin.....	1 : 4000	1 : 500	1 : 250	1 : 5000

The specific gravities are 0.9495 and 0.9607, respectively.

No difference is observable here either in the rate or extent of extraction.

The sample without glycerin has precipitated considerably, those with glycerin materially less. Sugar or glucose has not hindered precipitation in this preparation, but glycerin shows some effect.

Gentian.—The compound tincture was made with and without glycerin. (It may be noted here that glycerin was introduced into this preparation in the last revision.) Both showed an equal bitterness in dilutions of 1 : 2000. The specific gravities were 0.9870 and 0.9964, respectively. In color and general appearance they are indistinguishable.

All the samples have precipitated enough to form a film about the thickness of heavy paper on the bottom of the bottles, and there is no appreciable difference in the amounts. Neither glycerin nor sugar nor glucose appears to have diminished precipitation in this.

Sarsaparilla.—The U. S. P. Compound Fluidextract was made. The reserves were compared for color, taste and odor, both as received and in dilutions (for taste particularly) of 1 : 100, and no differences were noted. The fluidextracts appeared alike, and tested alike in dilutions of 1 : 500. The specific gravities were 1.0685 and 1.0885, respectively.

The sample containing no glycerin has precipitated considerably, those containing glycerin less, and those containing sugar and glucose still less—the last almost a trace. In this case glycerin materially retards precipitation, and so does sugar, the last being the more effective.

Stillingia.—The N. F. Compound Fluidextract was prepared. This is not an easily distinguishable preparation and comparisons were vague.

The fluidextracts appeared the same, as finished and also in dilutions of 1 : 2000.

The specific gravities were 1.0952 and 1.170, respectively.

This preparation contains the largest proportion of glycerin (25%) of any in this series, and a corresponding amount of sugar and glucose was used for comparison.

The sample containing the smallest amount of precipitate is the one containing no glycerin. This shows only a thin paper-like film on the bottom of the bottle. The one to which glycerin was added contains a little more, and that wherein glycerin was used in the menstruum two or three times as much. The sample containing sugar and glucose are much worse, showing a layer of two or three millimeters of sediment on the bottom of the bottle. None of these samples have been improved, in any respect, by glycerin or sugar.

Taraxacum.—The U. S. P. fluidextract was made and the fractions tested by taste as follows:

	1st fraction.	2nd. fraction	3rd. fraction	Fluidextract.
Glycerinated menstruum.....	1 : 800	1 : 150	1 : 40	1 : 1000
No glycerin.....	1 : 800	1 : 150	1 : 40	1 : 1000

No difference is shown here in the rate or extent of extraction. The fluidextracts had a specific gravity of 1.005 and 1.1227, respectively.

All the samples have precipitated in nearly equal amounts, showing about 1 millimeter of sediment on the bottom of the bottles. The sample without glycerin and the one with sugar appear a little heavier. Glycerin appears to have a slight retarding effect on precipitation but so slight as to be of no practical value in these samples.

Thyme.—The N. F. fluidextract was made. The taste is so mild in this preparation that a comparison of the fractions was not very satisfactory. The fluidextracts compared closely for odor and taste in dilutions of 1 : 500. The specific gravities were 1.087 and 1.0735, respectively.

Each of the samples has precipitated considerably, showing a layer of about 2 millimeters thickness on the bottoms of the bottles. Neither glycerin, sugar nor glucose shows any appreciable influence in this case.

Uva Ursi.—The U. S. P. fluidextract was made. This is another drug which is difficult to judge by physical properties because its fluidextract has no markedly characteristic odor or flavor and on dilution these are quickly lost. The fractions obtained all showed a distinct difference in color, those made without glycerin all being darker and also clearer. The finished fluidextracts likewise show a distinct difference in the same way—the glycerinated menstruum taking out less color. On dilution with water in proportion of 1 to 1000, the glycerinated preparation produces markedly less cloudiness than does the other. The odor and taste is also in favor of the no-glycerin preparation, but the difference here is slight. Neither of the dilutions has a very distinct odor or flavor. The evidence, however, distinctly points to a retarding action of the glycerin in extracting this drug.

The specific gravities of the two fluidextracts containing menstruum-glycerin and added-glycerin are 1.1085 and 1.1785, respectively, again indicating more complete extraction without glycerin.

Precipitation has occurred in all samples. The one without glycerin and the ones with sugar and glucose show about 3 millimeters of sediment, while the ones containing glycerin show a little less—about 2 millimeters. Glycerin, therefore, has retarded precipitation in this preparation.

SUMMARY.

Experiments have been conducted on 27 official preparations to ascertain the influence of glycerin on these, first as a menstruum, and second its influence on precipitation.

Final conclusion cannot be drawn from one series of experiments. Several experiments on each preparation, using different lots of drugs, are needed to establish the facts satisfactorily. The present series, however, clearly indicates that a distinction should be drawn between glycerin as a solvent in these preparations, and glycerin as a stabilizer. Sugar may act in the latter capacity quite as satisfactorily in some instances.

As a solvent, glycerin shows that it has retarded extraction in calisaya and hydrastis—two alkaloidal drugs—in rhubarb, geranium, and rose—drugs contain-

ing marked quantities of tannin and in apocynum and uva ursi. It has aided the extraction of red cinchona, butternut, hamamelis, krameria and nutgalls. The astringent drugs particularly appear to be favorable to the use of glycerin as a menstruum but they have not all acted alike in this respect. On the other drugs, glycerin shows no appreciable difference. That is, it neither helps nor hinders extraction, as shown in the results.

As a stabilizing agent, to prevent precipitation, glycerin is shown to be effective on ten of the drug preparations, *viz.*, red and yellow cinchona, geranium, hamamelis, hydrastis, krameria, nutgall, columbo, sarsaparilla compound and uva ursi. On the others it has shown no effect. And it may be remarked that in no case has glycerin been proved to entirely prevent precipitation in preparations which are prone to deposit. It is a fair inference that the value of glycerin for this purpose has been overestimated. Even in the case of cinchona preparations, in which its usefulness is unquestioned, hydrochloric acid appears to be of greater value than glycerin for stabilizing the preparations.

Sugar has been shown to hinder precipitation in preparations of calisaya, red cinchona, hamamelis, krameria, rose, apocynum and compound sarsaparilla. Its value is doubtfully indicated for butternut, hydrastis and geranium. In most instances it is shown to be less efficient than glycerin, part for part, but in two or three it appears to be more efficient.

While glycerin is found to reduce precipitation in ten drug preparations, sugar has acted similarly in nine. These correspond in six cases, and differ on the others. (Sugar was not tried on tincture of nutgalls because it is not appreciably soluble in the menstruum used.) Apparently glycerin acts by preventing changes in the fluids through light or air, rather than as a solvent.

Glucose acts similarly to sugar, but it introduces some water which changes the alcoholic strength, and it is thus less desirable.

But the fact should not be overlooked that of the 27 preparations tried, in which glycerin is directed by the Pharmacopoeia or National Formulary, only one-third of them show any advantage in the use of glycerin, while some of the others show a distinct disadvantage.

Only in the astringent drugs does it appear that glycerin is of value as a solvent, while as a stabilizer of galenical preparations the results suggest that other things may sometimes be preferable.

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ABSTRACT OF DISCUSSION.

ALBERT SCHNEIDER: Mr. Scoville's paper brings out very clearly the usefulness of the knowledge of colloidal chemistry in the study of the extraction of drugs. I would like to ask what the results of operators have been with Lloyd's reagent in making alkaloidal assays.

E. A. RUDDIMAN: I have used Lloyd's reagent in the analysis of syrups, containing alkaloids, but without success. The reagent extracts the alkaloids, but in my experience, it is a difficult matter to separate the extracted alkaloids from the reagent.
