for by the dentist at regular intervals, nor are they in the habit of using a tooth brush. Under these conditions dense calcific deposit may form around the gum margins and on the teeth. This is very difficult to remove. A solvent which will penetrate and soften such densely glazed calcific deposits would be of use to the dental profession. It must be taken into consideration that a solvent which would dissolve calcific deposits would also have a chemical action on the enamel of the teeth. However, a preparation in the hands of a skilful dentist would not come in direct contact with the enamel of the teeth.

Dry-sockets are of common occurrence in the practice of dentistry, and at times very difficult to restore as well as most painful to the patient. Help the dentist in your community solve his need for a treatment for dry-sockets.

The problems in dental pharmacy are numerous. We can only begin to realize the growing demand for dental pharmacy when we consider a national tentative curriculum in dentistry which includes subjects relating to treatment and diagnosis of abnormal conditions of the oral cavity as follows: Bacteriology, Preventive (Hygiene), Physiological Chemistry, Materia Medica, Physiology, Pharmacodynamics, General Pathology, Oral Medicine (Pulp Canal), Oral Pathology, Prevention (Nutrition), Diagnosis, Anesthesia, Oral Surgery, Oral Medicine, Principles of Medicine.

A curriculum including subjects as those mentioned gives us a picture of future dentistry. The dental profession is aware of the importance of their specialized branch of medicine in the prevention of disease and restoration of the teeth. We must contribute our part to the advancing profession if we are to maintain our recognition as professional men serving the needs of the correlated medical professions.

A STUDY OF VEHICLES FOR MEDICINES.*

BY BERNARD FANTUS, H. A. DYNIEWICZ AND J. M. DYNIEWICZ.

VIII. THE GLYCYRRHIZA VEHICLES.

That glycyrrhiza is a valuable disguising agent may be gathered merely from the extensive usage of at least some of its preparations. In Professor Gathercoal's (1) report this is given as follows:

	Usage per 10,000 Rs.
Syrup of Glycyrrhiza, N. F.	14.8
Fluidextract of Glycyrrhiza, U. S. P.	11.2
Elixir of Glycyrrhiza, U. S. P.	2.6
Fluidglycerate of Glycyrrhiza, N. F.	0.0
Aqueous Elixir of Glycyrrhiza, N. F.	0.0

The remarkable validity of this verdict of the medical profession, as expressed by the relative frequency of use of these preparations, will become clear by the perusal of this study.

* From the Laboratory of Pharmacology, University of Illinois, College of Medicine.

THE DISGUISING OF SALTY TASTES.

Experiment 1.

(*a*) Dissolve 0.5 Gm. of sodium bromide in 5 cc. of Syrup.
(*b*) Dissolve 0.5 Gm. of sodium bromide in 5 cc. of Fluidextract of Glycyrrhiza 1 part, water 3 parts.
(*c*) Dissolve 0.5 Gm. of sodium bromide in 5 cc. of Syrup of Glycyrrhiza.

Those who taste the resulting solutions would, we believe, be in favor of the syrup of glycyrrhiza (*1c*) solution. The bromide solution in syrup (*1a*) tastes more salty; and the saltiness lingers after the sweetness of the sugar has left the palate. The fluidextract (*1b*) gives but little sweetness when the liquid enters the mouth, so that the saltiness predominates at first. This is followed by a period of prolonged sweetness which outlasts the saltiness of the bromide. The Syrup of Glycyrrhiza combines the immediate sweetness of the sugar solution with the prolonged sweetness of the glycyrrhiza.

Experiment 2.

Ammonium chloride, 0.30 Gm. dissolved in 5 cc. each of the three different solvents as above, yields the same conclusion.

Experiment 3.

Potassium iodide, 0.30 Gm. dissolved in 5 cc. each of the above solvents, also verifies results obtained.

Conclusion: The Syrup of Glycyrrhiza is a better vehicle for halides (Experiments 1, 2 and 3) than is simple syrup or the Fluidextract of Glycyrrhiza.

COLLOIDALITY LESSENS TASTE SENSATION.

This disguising power of glycyrrhiza for saltiness appears to be more than a mere matter of sweetness because there seems to be less saltiness in the taste of, *e. g.*, the bromide glycyrrhiza preparations than in equivalent solutions not only in simple syrup, but also in such flavoring syrups as the Syrup of Raspberry and the Compound Syrup of Sarsaparilla. There is apparently a loss of saline ions as far as taste sensation is concerned; and we attempted, by means of numerous experiments, to determine the reason for this loss.

One's first guess might be that the colloid interfered with diffusion of the crystalloid. True, established theory does not support this assumption. We, nevertheless, performed diffusion experiments (using collodion and celloidin sacs) with methylene blue solution and conducted similar studies with bromide. Whenever a difference was noted, this could always be ascribed to a leaky diffusion membrane. We also studied the modification in the development of "Liesegang's rings" (2) produced by colloid; but likewise without sufficiently striking results. That merely a difference in the rate of diffusion could hardly be the cause for the difference in taste might also have been obvious from the fact that the taste sensation is experienced immediately, while diffusion is a relatively slow process, at least as far as enabling one to demonstrate a difference by the experiments carried out.

It may be that differences in surface tension might explain this interference with taste sensation. Or, possibly, it might be due to adsorption of the saline ions by the colloid: it being well known that, when colloid is present, it is most difficult to re-

move the last traces of salt ions by diffusion. No matter how the colloid acts, it is evident that *colloidality has disguising value.*

THE BEST SOLVENT IS THE BEST VEHICLE.

To test the disguising value of the Syrup of Glycyrrhiza as compared with the elixirs, we prepared the following solutions:

Experiment 4.

(*a*) Dissolve 0.5 Gm. of sodium bromide in 5 cc. of Syrup of Glycyrrhiza.
(*b*) Dissolve 0.5 Gm. of sodium bromide in 5 cc. of Elixir of Glycyrrhiza.
(*c*) Dissolve 0.5 Gm. of sodium bromide in 5 cc. of Aqueous Elixir of Glycyrrhiza.
(*d*) Dissolve 0.5 Gm. of sodium bromide in 5 cc. of Aromatic Elixir.

We believe that again the verdict would be in favor of the Syrup of Glycyrrhiza as compared with all of the elixir preparations. The solution in Aqueous Elixir of Glycyrrhiza is less offensive than the solution in the Elixir of Glycyrrhiza and this is less offensive than the solution in the aromatic elixir. It will be found that the bromide solution in syrup (*1a*) is more pleasant than are any of the alcoholic solutions, even though they contain glycyrrhiza; and the salty taste becomes progressively more noticeable with increase in alcohol concentration. The probable explanation for the superiority of the aqueous over the alcoholic vehicle is to be found in the insolubility of sodium bromide in alcohol. Evidently the presence of alcohol in the elixir makes the latter a poorer solvent than the watery medium of the tongue and palate. It is well known that, when two different solvents compete for the same solute, the latter will rapidly enter the better solvent in greater proportion than the poorer solvent. We might imagine, therefore, that the saline is quickly drawn from the alcohol containing solution into the more congenial aqueous medium of the mucous membrane. The reason, probably, why the aqueous elixir of glycyrrhiza (containing less than 5% of alcohol) is so distinctly inferior in its disguising power for saline taste, lies in the relatively small proportion of glycyrrhiza contained in it. We, therefore, believe that *it is a mistake to use elixirs for the disguising of water-soluble alcohol-insoluble salines.* The relative disguising inefficiency of the aqueous elixir of glycyrrhiza as well as its very limited use justify the suggestion that it be deleted. On the basis of observations such as the above and numerous others, we believe to be justified in pronouncing that, other things being equal, *the best solvent is the best vehicle.* Conclusion: the taste of the bromide in elixir is more offensive than that of a solution of bromide in Syrup of Glycyrrhiza.

THE DISGUISING OF THE BITTER TASTE.

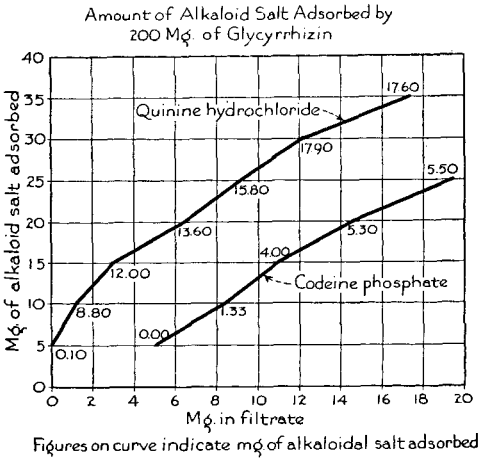
Experiment 5.

(*a*) Dissolve 0.025 Gm. of codeine phosphate in 5 cc. of Syrup.
(*b*) Dissolve 0.025 Gm. of codeine phosphate in 5 cc. of Syrup of Glycyrrhiza.
(*c*) Dissolve 0.025 Gm. of codeine phosphate in 5 cc. of Aromatic Syrup of Eriodictyon.
(*d*) Dissolve 0.025 Gm. of codeine phosphate in 5 cc. of Fluidextract of Glycyrrhiza and water, equal parts.
(*e*) Dissolve 0.025 Gm. of codeine phosphate in 5 cc. of Elixir of Glycyrrhiza.

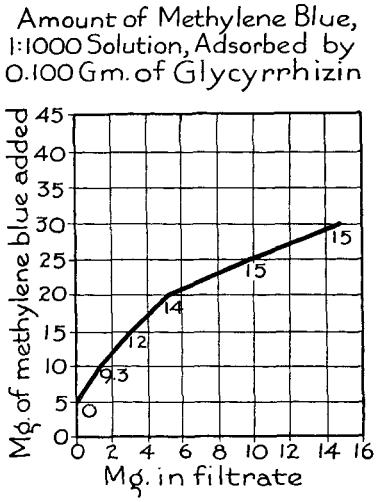
Again the solution in Syrup of Glycyrrhiza (*5b*) merits first place as far as palatability is concerned. The Aromatic Syrup of Eriodictyon probably comes next

in order of pleasantness; but it is quite evident that the amount of codeine phosphate (0.025 Gm.) exceeds the precipitating, hence the disguising power of the eriodictyon preparation. In a previous study (3) we have found that 5 cc. of the Aromatic Syrup of Eriodictyon were capable of disguising 0.008 Gm. of codeine phosphate. The subjoined Graph 1 gives the amount of codeine phosphate removed by glycyrrhizin from solutions of various strengths. It shows that the adsorption power of glycyrrhizin for codeine is rather limited and definitely less than that of the resin of eriodictyon (cf. 3). Nevertheless, its disguising power is obviously superior to that of eriodictyon, which must be due to the prolonged after sensation of sweetness produced by the glycyrrhizin, which is considered 150 times sweeter than sugar.

As to the removal of quinine from solution, adsorption experiments (Graph 1) show glycyrrhizin to be again decidedly inferior to the eriodictyon resin, as it also



Graph 1.



Graph 2.

is in regard to the adsorption of methylene blue from solution (Graph 2). This is likewise borne out by tasting experiments. Thus, a suspension of quinine ethyl carbonate (euquinine) in Syrup of Glycyrrhiza, while pleasant at first, becomes bitter soon thereafter and a prolonged bitter aftertaste is left. Similarly, one-fourth or one-half mg. of strychnine sulphate added to Syrup of Glycyrrhiza, while pleasant at first, leaves a lingering bitter aftertaste. We must conclude, therefore, that the Syrup of Glycyrrhiza is inferior to the Aromatic Syrup of Eriodictyon for the disguising of the bitter taste of alkaloids. Neither glycyrrhiza nor eriodictyon are of any value for the disguising of the bitter taste of aloin.

THE DISGUISING OF THE ALKALINE TASTE.

Experiment 6.

Dissolve (*a*) 0.60 Gm. of potassium carbonate in 0.3 cc. of water and add 5 cc. of Syrup.
(*b*) Repeat above and add Syrup of Glycyrrhiza instead of the Syrup.
(*c*) Repeat above and add Aromatic Syrup of Eriodictyon instead of the Syrup.

Again the Syrup of Glycyrrhiza gives the most pleasant disguise.

THE DISGUISING OF THE SOUR TASTE.

For the disguising of the sour taste glycyrrhiza is, of course, unsuitable, as the glycyrrhizin is precipitated by acid.

VARIABILITY OF GLYCYRRHIZA PREPARATIONS.

In view of the great disguising value of glycyrrhiza, the well-known variability of its preparations seems most unfortunate. It is common experience, in their prescribing, that some patients like the medicine, while others complain of its "nastiness." That this is not due to taste idiosyncrasies of individuals, but to variability of the glycyrrhiza preparations, is suggested by the fact that patients sometimes complain the medicine tasted differently on refilling, as though the druggist "had made a mistake." Our studies show that there is actually an enormous difference between the palatability of supposedly equivalent preparations bought in the open market, as well as between preparations made in our laboratory by identical methods from different samples of the drug.

TASTES OF VARIOUS SPECIMENS OF FLUIDEXTRACT OF GLYCYRRHIZA.

Specimen.	Prepared.	Taste.
1	In Laboratory	Sweet, slightly bitter
2	In Laboratory	Sweet, quite bitter
3	By Firm No. 1	Bitter, slightly sweet
4	By Firm No. 2	Bitter-sweet
5	By Firm No. 3	Bitterish and flavor of scorching
6	By Firm No. 4	Sweet, slightly bitter

Analogous differences were found in the Syrups of Glycyrrhiza made from these fluidextracts.

SYRUP OF GLYCYRRHIZIN.

The great variability of the glycyrrhiza preparations and the generally acknowledged difficulty of standardizing them, seems to us so serious an obstacle to their use as flavoring vehicles, that we undertook a great deal of experimentation with the view of discovering a method that would always yield a uniformly pleasant product. We started these experiments with the active principle, glycyrrhizin. The proportion of glycyrrhizin in glycyrrhiza is very variable, ranging from 6–14%. No wonder, we thought, there is such variation in the taste of the glycyrrhiza products. When we realize that, in addition to this, the sweetness of glycyrrhiza depends to a great extent upon the relative proportion of alkali metal, such as potassium, calcium or ammonium, with which the glycyrrhizin is associated, we can readily appreciate a reason for the difference in the taste of various specimens of rhizome from different sources as well as when they are kept in different ways. It seems that some specimens of rhizome have undergone an actual souring from improper preservation. We have found that the glycyrrhizin itself in such rhizomes is not changed, for though separated from even the bitterest fluidextract or rhizome, it is still capable of yielding a perfectly sweet product by combination with the proper amount of alkali. Inasmuch as glycyrrhiza contains about 3% of a bitter principle, which is certainly undesirable in a vehicle intended to disguise a

bitter taste, it seemed quite logical to prepare the Syrup of Glycyrrhiza from the active principle, just as we no longer prepare syrup by extracting and evaporating beet juice or sugar cane juice.

We found that the ammoniated glycyrrhizin is not as pleasantly sweet nor as colloidal as a more acid combination, *i. e.*, one containing a smaller relative proportion of ammonium hydroxide. After experimenting with various proportions of glycyrrhizin and diluted ammonia water, the best results were secured by a proportion of 1 part of glycyrrhizin to 4.5 parts of $N/10$ ammonium hydroxide. This yields so colloidal a liquid that a syrup made with 1% of the glycyrrhizin thus prepared becomes gelatinous. Owing to this high degree of colloidality we cannot employ more than $^1/_2$% of the glycyrrhizin in this combination. This is from $^1/_3$ to $^1/_7$ the amount of glycyrrhizin in its native, less colloidal state in the syrup made from the fluidextract. And yet this syrup of glycyrrhizin is quite efficient in the disguising of salines. This might serve as another proof of the idea, previously expressed, that it is the colloidality upon which the disguising power of these preparations for salines partly depends.

We employed the following formula for the preparation of the syrup of glycyrrhizin:

SYRUP OF GLYCYRRHIZIN.

Glycyrrhizin	**5.0 Gm.**
***N*/10 Ammonium Hydroxide Volumetric Solution**	**22.5 cc.**
Distilled Water	**40.0 cc.**
Syrup, a sufficient quantity	
To make	**1000.0 cc.**

Triturate the glycyrrhizin with the distilled water and, while actively triturating, add the $N/10$ ammonium hydroxide and triturate until solution is effected. Then add enough of the syrup to make 1000 cc. and mix thoroughly.

At first thought this formula might be criticized as too expensive for consideration, owing to the high market price of glycyrrhizin, which is quoted at $4.40 a pound, or let us say, at about one cent per Gm. This would, however, make the glycyrrhizin cost five cents per 1000 cc. of the syrup, as against over sixty cents for the fluidextract or seventy cents for the fluidglycerate, which shows that the syrup of glycyrrhizin actually costs one-twelfth as much as far as the glycyrrhiza addition is concerned. Inasmuch as glycyrrhizin could not be secured in the market, we prepared it either from the ammoniated glycyrrhizin or, what is much more economic, from the drug itself. For this purpose, a concentrated aqueous percolate is acidified with hydrochloric acid. The precipitate is washed by repeated decantation until free from chloride ions, as indicated by Silver Nitrate T.S., and dried at moderate temperature.

Unfortunately, the Syrup of Glycyrrhizin is so colloidal that it is "salted out" by the addition of bromide, which makes it turbid immediately and causes a deflocculation of the glycyrrhizin on standing. We have not yet succeeded in determining what it is that keeps the glycyrrhizin from deflocculation when saline is added to a preparation made from the fluidextract. Inasmuch as ammoniated glycyrrhizin, which is less colloidal, is also deflocculated, there is probably another reason than a difference in the relative proportion of glycyrrhizin and alkali. We attempted to discover what it was in the extractives that kept from deflocculа-

tion the glycyrrhizin in the syrup of glycyrrhiza, by adding the residue left after separation of the glycyrrhizin from extract of glycyrrhiza. This, however, failed to stabilize the preparation. It must be that the protective principle is denatured by the acid used in the separation of the glycyrrhizin.

We believe that the syrup of glycyrrhizin has decided merit and that it might ultimately replace the cruder product, providing it can be suitably stabilized. Owing to the advanced state of development of the forthcoming U. S. P. and the N. F. revisions, we desire to have the privilege, which we also grant freely to others, to make further observations with syrup of glycyrrhizin before advocating introduction of a formula for it in one of our official books.

AN IMPROVED FLUIDEXTRACT OF GLYCYRRHIZA.

In the present state of the glycyrrhiza situation, it seems that we must concentrate our efforts upon minimizing the nastiness and the variability of the glycyrrhiza preparation from which the Syrup of Glycyrrhiza is to be made. It is, in point of fact, being prepared from the fluidextract now, even though the N. F. specifies that it be made from the fluidglycerate. The reason we believe this to be the case is that the fluidglycerate is not kept in drug stores; that, indeed, it is not even upon the market; and that manufacturers had to prepare it specially for us when we insisted upon ordering it. As the specimens of fluidglycerate are just as variable as are those of the fluidextract, it presents no advantage from this standpoint; and furthermore it does not keep as well. For these reasons, and especially on the basis of non-use we propose that the fluidglycerate be deleted from the National Formulary.

It seems that the standardization of the Fluidextract of Glycyrrhiza from the standpoint of glycyrrhizin assay presents considerable difficulty as may be gathered from the literature on the subject (4–11). The simple methods are unreliable and the reliable methods, complicated. Nevertheless, it should be easily possible to lessen the variability of the preparation, at least as far as the content of solid extractive is concerned. This in preparations we have tested ranged between 20 and 30 per cent, as is shown by Table I.

TABLE I.—PERCENTAGE OF SOLID EXTRACT AND OF GLYCYRRHIZIN IN VARIOUS SPECIMENS OF FLUIDEXTRACT OF GLYCYRRHIZA.

	Per Cent of Solid Extract.	Per Cent of Glycyrrhizin in Extract.	Per Cent of Glycyrrhizin in Fluidextract.
Specimen 1	30	24.6	7.38
Specimen 2	27	24.2	6.54
Specimen 3	26	19.5	5.09
Specimen 4	25.7	23.1	5.94
Specimen 5	20	24.9	4.98
Specimen 6	23	..	..
Specimen 7	25.4	..	..
	Av. 25.3		Av. 5.98

NOTE: We were unable to determine the amount of solid extract in two other commercial samples because they failed to dry after heating for five days. The same difficulty was experienced with a fluidextract prepared in our laboratory by the U. S. P. IX method, in which ammonia water was employed.

It will be noted from Table I that, even though the amount of solid extract varied from 20 to 30 per cent, the average was practically 25 per cent. It is of interest to note that the amount of glycyrrhizin present was in four of the instances exactly one-fourth the quantity of the dry extract. For practical purposes, therefore, standardization in accordance with the amount of dry extract present in the fluidextract might suffice and the figure should be placed at 25 per cent.

There are two ways by which we might develop a fluidextract of Glycyrrhiza of standard solid extract content.

1. Exhaust the drug and concentrate the percolate to a somewhat greater extent than the ultimate bulk that the finished preparation is to have. By determining the quantity of the solid extract in a portion of the liquid thus obtained and adding enough fluid to bring the total solid residue content up to the standard, the desired result would be secured. What complicates the situation and makes the method just discussed unsuitable for the purpose is that the Fluidextract of Glycyrrhiza contains 25 per cent of alcohol and that the alcohol when added to the percolate produces a precipitate which is filtered out after sedimentation and decantation. The alcohol would either have to be added before the final concentration, in which case it would be difficult to secure a standard proportion of alcohol in the finished product, or else the alcohol would have to be added after standardization in which case it would render the previous determination invalid as the alcohol removes additional solid material from the preparation.

2. The other method would be to dissolve the pure extract of glycyrrhiza, which contains a variable quantity (about 25%) of moisture, in a certain quantity of water, an amount small enough so that the concentration will be excessive and dilution be required, adding the alcohol, separating the precipitate by sedimentation, decantation and filtration. Then the percentage of dry residue is determined in a small portion of the fluid, and the bulk is brought to the required amount to make the finished preparation carry 25 per cent of extractive by the addition of a sufficient quantity of a mixture of alcohol 1 part and water 3 parts. This is obviously the method to be chosen.

We, therefore, propose the following method for the preparation of the Fluidextract of Glycyrrhiza, which we would like to submit to the U. S. P. Revision Committee for consideration.

FLUIDEXTRACTUM GLYCYRRHIZÆ.

Fluidextract of Glycyrrhiza.

Fldext. Glycyrrh. Fluidextract of Licorice Root.

The Fluidextract of Glycyrrhiza contains not less than 24% and not more than 26% of dry extractive. The preparation should be of intensely sweet taste with but a slight tinge of bitterness, having the characteristic odor of glycyrrhiza and it should be free from even a suggestion of having become scorched in its preparation.

Extract of Glycyrrhiza, Pure ..... **400.0 Gm.**
Alcohol
Water, of each a sufficient quantity

Dissolve the pure extract of glycyrrhiza with the aid of the water-bath in enough water to make the solution measure 750 cc. Then add 250 cc. of alcohol and agitate the mixture. Set aside for 7 days, decant the clear liquid and filter the remainder. Determine the amount of solid extractive in 5 cc. of the liquid thus obtained by drying to constant weight. From the weight obtained calculate the number of grams per 100 cc. Calculate the quantity of solid extractive in the total quantity of liquid and add enough of a mixture of alcohol one part and water three parts to make the finished preparation contain exactly 25% of solid extract.

In explanation of the process advocated it might be pointed out that the extract of glycyrrhiza should contain 25% of moisture; but that it may contain more or less. In starting with an excess of the extract we save ourselves a preliminary determination of the dry extractive contained in it. When we dissolve 400.0 Gm.

of extract in 750 cc. of water, we are certain that dilution will be ultimately required, so that we may add 250 cc. of alcohol, confident that this will not be an excess, as the finished preparation will measure more than 1000 cc.

AN IMPROVED EXTRACT OF GLYCYRRHIZA.

We owe Dr. Percy A. Houseman the important information that the bitter principle of glycyrrhiza is extracted in much greater proportion toward the end of the percolation than in the beginning. Before having been apprised of this we made the observation, without realizing its significance, that when we tasted the first portions of a percolate we thought we would this time get a very palatable product; only to be bitterly disappointed by the bitterness of the final preparation.

When, for instance, we subject 200 Gm. of glycyrrhiza to percolation, according to the directions of the U. S. P.; but separate each successive 100-cc. portion, we secure fractions with a progressively decreasing amount of dry extractive in each as shown in Table II.

TABLE II.

Percolate.	Dry Extractive.	Taste.
100-cc. portion 1	8.2188 Gm.	Sweet
..... 2	9.3195 Gm.	"
..... 3	6.2855 Gm.	"
..... 4	5.0567 Gm.	"
..... 5	4.3387 Gm.	"
..... 6	4.3613 Gm.	Sweet, slightly acrid
..... 7	3.7498 Gm.	"
..... 8	2.7183 Gm.	"
..... 9	2.2088 Gm.	"
..... 10	1.8353 Gm.	Offensively acrid
..... 11	1.2655 Gm.	" worse
..... 12	0.8989 Gm.	"
..... 13	0.6730 Gm.	"
..... 14	0.5160 Gm.	"
250-cc. final portion	1.1152 Gm.	Bad
Total 1650 cc.	52.5613 Gm. =26.28%	

It will be noted that the first 500 cc. yield 33.2192 Gm. of extractive or 16.6%, which is 63% of the total extractive, and has a sweet taste devoid of acridity.

We, therefore, advocate consideration by the U. S. P. Revision Committee of the following formula for the Pure Extract of Glycyrrhiza.

EXTRACTUM GLYCYRRHIZÆ.

Pure Extract of Glycyrrhiza.

Ext. Glycyrrh. Pur. — Pure Extract of Licorice Root.

Glycyrrhiza, in coarse powder ..... **1000 Gm.**
Boiling water, a sufficient quantity

Moisten the drug with boiling water, and macerate in a covered container in a warm place for two hours. Transfer the moist drug to a metal percolator (not iron) and percolate with boiling water until a yield of not over 150 Gm. of extract on a dry basis is obtained, which is likely to be secured in the first 2500 cc. of percolate. Evaporate this percolate promptly on a water-bath. Not over 200 Gm. of extract containing 25% moisture should be obtained.

ALTERNATIVE FORMULA FOR AN IMPROVED FLUIDEXTRACT OF GLYCYRRHIZA.

Should an alternative formula for the improved Fluidextract of Glycyrrhiza be desired in which the preparation is to be made from the crude drug, the following procedure might be considered.

FLUIDEXTRACT OF GLYCYRRHIZA.

Alternative Formula.

Glycyrrhiza, in coarse powder	**1000 Gm.**
Alcohol	
Water, a sufficient quantity	

Moisten the glycyrrhiza with 5000 cc. of boiling water, mix thoroughly, and allow it to macerate in a covered container in a warm place for two hours. Then transfer the moist drug to a tinned or enameled percolator, and allow the percolation to proceed, gradually adding boiling water until 2500 cc. are obtained. Evaporate the percolate on a water-bath or steam-bath to 300 cc. and when cold add 75 cc. of alcohol and mix thoroughly. Allow the product to stand for seven days in a stoppered container, then decant the clear liquid, filter the remainder, and wash the residue on the filter with a sufficient quantity of a mixture of alcohol 1 part and water 3 parts to make the fluidextract measure 400 cc.

Determine the amount of solid extractive in 5 cc. of the liquid thus obtained by drying to constant weight. From the amount obtained calculate the number of grams per 100 cc. Calculate the quantity of extractive in the total quantity of liquid and add enough of a mixture of alcohol 1 part and water 3 parts to make the finished preparation contain 25% of solid extract.

A "PALATABLE" SOLUTION OF CHLORAL HYDRATE.

The disguising value of the Fluidextract of Glycyrrhiza is illustrated by the following prescription which yields the least offensive liquid administration form of chloral hydrate that we are acquainted with.

℞ Chloral Hydrate	15.0	Gm.
Gluside	0.06	Gm.
Fluidextract of Glycyrrhiza	30.0	cc.
Syrup of Orange, to make	60.0	cc.

M. and label: Teaspoonful in water at bedtime.

The addition of sodium bromide is admissible as shown by the following prescription:

℞ Chloral Hydrate	7.5	Gm.
Sodium Bromide	15.0	Gm.
Water	15.0	cc.
Gluside	0.06	Gm.
Fluidextract of Glycyrrhiza	30.0	cc.
Syrup of Orange, to make	60.0	cc.

AROMATIC SYRUP OF GLYCYRRHIZA.

We deplore the crudeness of the formula for the Syrup of Glycyrrhiza at present official in the N. F. Not only is there no possibility whatever for the prescriber to know whether the patient will receive a moderately pleasant or a nasty preparation; but, even granted that the most palatable glycyrrhiza product is used, the mere addition of syrup to it does not yield as pleasant a preparation as could easily be secured by the use of a little flavoring. Every candy and chewing-gum manufacturer knows that the glycyrrhiza flavor needs to be improved by an anise bouquet. Our formulary does not make use of this knowledge. In experimenting to determine the most desirable flavor of glycyrrhiza, we find, after a trial of many

different formulas and proportions, that the anise flavor by itself is not sufficiently pleasing to be satisfactory. It is much improved by the addition of a suitable proportion of oil of fennel. If equal parts of oil of anise and oil of fennel are mixed, the anise flavor is almost completely overwhelmed by the fennel. The most acceptable proportion seems to be: 7 parts of oil of anise and 1 part of oil of fennel. Even this combination is not perfectly satisfactory. It has what might possibly be called a "musty" smell. In looking over formulas for anise bouquets, we find that this evidently is very generally recognized, for all such formulas contain some additional flavor, the function of which seems to be to add "liveliness" to the bouquet. We find oil of bitter almond, oil of spearmint and even nitrous ether used for this purpose. To us the bouquet of the N. F. Elixir of Anise seems to be the most desirable.

SYRUPUS GLYCYRRHIZÆ AROMATICUS.

Aromatic Syrup of Glycyrrhiza.

Syr. Glycyrrh. Arom.

Oil of Fennel	0.05	cc.
Anethol	0.50	cc.
Benzaldehyde	0.015	cc.
Fluidextract of Glycyrrhiza	250	cc.
Syrup, a sufficient quantity, to make	1000	cc.

Add the volatile oils to the Fluidextract of Glycyrrhiza and agitate until thoroughly mixed. Then add enough of syrup to make the product measure 1000 cc.

BROMIDE SYRUPS.

To the prescribing physician these studies yield the practical result that Syrup of Glycyrrhiza, especially in its improved form, the Aromatic Syrup of Glycyrrhiza, yields a palatable preparation, when used as vehicle for bromide. One might, therefore, suggest the following prescription.

℞ Sodium Bromide	30.0	Gm.
Water, just enough for solution or	30.0	cc.
Aromatic Syrup of Glycyrrhiza to make	120.0	cc.

M. and label: Teaspoonful in milk after meals and at bedtime.

A parenthetic note might not be amiss, in this connection, to explain the consideration underlying the second line of the above prescription. It is, of course, understood that the Syrup of Glycyrrhiza will not dissolve any considerable quantity of salt. It is also well known that syrups are relatively permanent only as long as they are saturated solutions. It is, therefore, necessary to add the minimal quantity of water that will dissolve the bromide so as to secure solution without dilution. The determination of this quantity might well be left to the pharmacist who if necessary can easily refresh his memory as to the solubilities by consulting his reference books, while it is hardly to be expected that the physician should carry these figures in his mind.

In this connection we would like to call attention to the joint responsibility of physician and pharmacist in the direction of delivering to the patient preparations that will keep without decomposition at ordinary room temperature. It happens not infrequently that a medicine that lasts for several days or more has undergone fermentation and become effervescing, even to the extent as to blow out the stopper.

Should this happen and the spoiled preparation be thrown away, it is even more fortunate than to have such a spoiled liquid forced down a child's unwilling throat, with possibly resultant digestive upset.

INCOMPATIBILITIES.

It might not be amiss at this point to recall to mind that glycyrrhiza has some of the following incompatibilities.

1. Acids, which precipitate the glycyrrhizin and destroy much of its sweetness.
2. Alkalies which destroy the colloidality of the preparation.
3. Heat which precipitates the glycyrrhizin.
4. Ionized iron compounds, because of resultant colloidal precipitate. Slightly ionized iron salts like iron and ammonium citrate may be added without precipitation.

CONCLUSIONS.

1. Glycyrrhiza is especially useful for the disguising of salines given in moderate dosage.
2. It is generally less efficient than eriodictyon for the disguising of the taste of alkaloids.
3. It is of but limited efficiency in the disguising of alkalies.
4. Its disguising power is due to the colloidality and the sweetening property of glycyrrhizin.
5. The Syrup of Glycyrrhiza is the most eligible of the glycyrrhiza preparations for disguising purposes in general.
6. The N. F. Syrup of Glycyrrhiza could be very much improved by an anise bouquet and we advise its introduction and the change of the title to "aromatic syrup of glycyrrhiza."
7. Owing to variability in the glycyrrhiza rhizome, which may result in a bitter instead of a sweet preparation, formulas for an improved Extract of Glycyrrhiza and Fluidextract of Glycyrrhiza have been elaborated, and are submitted for possible inclusion in the Pharmacopœia.
8. Other things being equal, the best solvent is the best vehicle. Hence it is an error to add alcohol to water-soluble, alcohol-insoluble saline, such as bromide. The taste of the bromide elixirs is more offensive than that of bromide syrups.
9. The Fluidglycerate of Glycyrrhiza should be deleted from the National Formulary, and also the Aqueous Elixir of Glycyrrhiza, as neither of them are employed to a sufficient extent to justify their retention.

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