

from the formula, (2) that the acid in the glycerite might well be omitted for the same reason, and (3) that it be recommended that at least the third class of preparations be prepared extemporaneously only.

#### DISCUSSION:

C. M. Snow: We have carried out some work on pepsin preparations, using saccharin and glycerin in place of sugar and alcohol. These preparations deteriorated more readily than our present official ones. The low alcohol content elixirs are suitable for pepsin preparations, though it is desirable that they be freshly made. In the light of these findings it would seem that the logical procedure would be to reduce the acid in the glycerite pepsin and prepare the pepsin elixirs extemporaneously from the glycerite. Incidentally it may be mentioned that investigations in our laboratories here demonstrate beyond any doubt that the Compound Elixir of Almond as a vehicle for the pepsin elixirs should replace Aromatic Elixir since the pepsin elixirs at the present time contain about 17½ per cent. of alcohol, while the same elixirs with Compound Elixir of Almond as a vehicle would reduce the alcohol content to 3½ per cent. without in any way tending to make the product more subject to fermentive changes.

### FERMENTATION EXPERIMENTS ON ELIXIRS OF LOW ALCOHOLIC CONTENT.\*

BY E. N. GATHERCOAL AND VIVIAN J. STUHLIK.

A number of the low alcoholic galenicals were inoculated with the mold *Penicillium glaucum*, the yeast *Saccharomyces cerevisiae* and *Bacillus subtilis* and kept in the incubator at 30° C. for seven days with the following results.

	Alcohol content.	Mold.	Yeast.	Bacillus.
Compound Elixir of Almond.....	5.0%	—	—	—
Elixir of Pepsin (proposed for N. F. V).....	3.5%	+	—	—
Elixir of Pepsin N. F.....	17.5%	+	—	—
Aqueous Elixir of Glycyrrhiza N. F.....	3.5%	+	—	—
Compound Elixir of Cardamom N. F.....	10.0%	+	—	—
Beef Bouillon.....	None	+	+	+
Glucose Solution.....	None	+	+	+
Litmus Milk.....	None	+	+	+

Similar inoculations of each preparation with each fungus were kept at room temperature, approximately 20° C., for ten days with exactly similar results except that the mold growths were not quite so conspicuous.

### DOSE STANDARDIZATION OF ELIXIRS.†

BY BERNARD FANTUS, M.D.

As a glance at the accompanying table will show, no uniform policy prevails at present in regard to the dosage of medicaments in the N. F. elixirs. In most cases the dose is a good deal smaller than the U. S. P. average dose; in one case it is equal (Elixir Cascara Sagrada) and in a few cases larger than the U. S. P. dose, *e. g.*, twice the U. S. P. dose in the case of elixir of phosphorus. The dose of the finished medicated elixir varies from a teaspoonful to two teaspoonfuls and even a tablespoonful. One may well wonder how such confusion originated. The

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† Abstracted from the address before the Unofficial Conference of U. S. P. and N. F. Revision Workers at Chicago, January 12, 1924.

explanation for this anomalous state of affairs is generally to be found in the solubility limitations of aromatic elixir.

With the view of overcoming this condition, which might militate against the popularity of the N. F. elixirs with physicians, the Subcommittee on Dosage (Dunning, Seltzer, Fantus) submitted the following resolution to the General Revision Committee, which accepted it:

"Whenever practicable, the dosage of the N. F. elixir is to be so adjusted as to make it carry an average pharmacopœial or N. F. dose per teaspoonful. This should not be accomplished except in special instances when it is impracticable to avoid doing it, by changing the character of the elixir. Furthermore, in the application of this principle each elixir should be considered separately."

The question then arises to what extent this proposition can be profitably applied. It is very doubtful whether it can or should apply to the compound elixirs. In case, *e. g.*, of the elixir of three bromides, the dose of each is 0.32 Gm. or about 1 Gm. of total bromide to the teaspoonful. As all these bromides act alike, the average dose of 1 Gm. of each would give a total of three times the average dose of bromide. Although no doubt a thorough scientific study of the dosage of the compound elixirs would be desirable, owing to the magnitude and difficulty of the task involved, attention has been, for the present, focused upon the elixirs containing single medicaments.

Name of elixir.	DOSAGE IN SIMPLE MEDICATED N. F. (IV) ELIXIRS.						
	Dose of official medicament per dose.	U. S. P. or N. F. av. dose.	Solubility.		Required change in vehicle elixir.		
			Water.	Alcohol.			
Ammonium bromide	0.34 Gm. per 1 teaspoonful	1 Gm.	1.3	12		Aqueous	
Ammonium valerate	0.14 Gm. per 1 teaspoonful	0.5 Gm.	0.3	0.6		No change	
Buchu (fldext.)	0.50 cc. per 1 teaspoonful	2. cc.	Insol.	Sol.		Alcoholic	
Cascara Sagrada (fe.)	2. cc. per 1 teaspoonful	2. cc.				No change	
Ferric phosphate	0.14 Gm. per 1 teaspoonful	0.25 Gm.	Sol.	Insol.		Aqueous	
Ferric pyrophosphate	0.14 Gm. per 1 teaspoonful	0.25 Gm.	Sol.	Insol.		Aqueous	
Gentian (fldext.)	0.14 cc. per 1 teaspoonful	1 cc.	Diluted	Alcohol		Alcoholic	
Guarana (fldext.)	0.8 cc. per 1 teaspoonful	2 cc.	1 plus	3		Aqueous aa	
Lithium bromide	0.68 Gm. per 2 teaspoonful	1 Gm.	Freely sol			Alcoholic 3	
Lithium salicylate	0.68 Gm. per 2 teaspoonful	1 Gm.	Very sol.			Aqueous 1	
Pepsin (glycerite)	0.8 cc. per 2 teaspoonful	3 cc.	50	insol.		Aqueous	
Phosphorus	0.001 Gm. per 1 teaspoonful	0.0005 Gm.	{ Alm.	400		No change	
Potassium acetate	1.275 Gm. per 4 teaspoonful	1	{ Insol.	2.9		Aqueous	
Potassium bromide	1.4 Gm. per 2 teaspoonful	1		250		Aqueous	
Sodium bromide	1.4 Gm. per 1 teaspoonful	1		16		Aqueous	
Sodium hypophosphite	0.14 Gm. per 1 teaspoonful	1		Sol.		Aqueous	
Sodium salicylate	0.34 Gm. per 1 teaspoonful	1		9.2		Aqueous	
Terpin hydrate	0.07 Gm. per 1 teaspoonful	0.25		13		Alcoholic	

In carrying out the principle that each teaspoonful of elixir shall contain one average dose of medicament, it will be necessary to change the vehicle in quite a number of instances. For example, potassium bromide is soluble one part in 250 parts of alcohol, and one part in 1.5 parts of water. If the elixir is to contain one gram of potassium bromide in 4 cc. of the vehicle, it is evident that the vehicle must be markedly aqueous in nature. On the other hand, terpin hydrate is soluble one part in 13 parts of alcohol and one part in 200 of water. Hence, the elixir vehicle

must be strongly alcoholic, as 0.25 Gm. of the drug is to be dissolved in 4 cc. of vehicle. Another illustration of the need for a strongly alcoholic elixir vehicle is the elixir of buchu. Upon the addition of fluidextract of buchu to the aromatic elixir of the present formula, a marked precipitation of the oils and resins of buchu takes place; and, when this has been filtered out, the resulting elixir bears hardly more than the flavor of buchu.

Since the introduction into the N. F. of aqueous elixirs, the limitation of dosage by solubility in alcohol can be readily overcome by the use of that aqueous elixir which best disguises the particular medicament. This, *e. g.*, in the case of bromides, we have found to be the aqueous elixir of glycyrrhiza. The need for a strongly alcoholic elixir would be met by a formula for an elixir containing 95% alcohol flavored by compound spirit of orange and sweetened with saccharin, which has been submitted to the general revision committee.

The objection has been raised against the use of the low alcohol (6 to 10 per cent. of alcohol) elixirs of the N. F. as vehicles for medicaments on account of the tendency of those elixirs to ferment, especially when frequently exposed to the air and when kept in warm rooms or warm climates. In answer to this objection it may be stated that in a number of these medicated elixirs, the medicament tends to preserve the elixir against fermentation. Further, even if it is not possible for manufacturers to place some of these medicated elixirs on the general market, there is no reason why formulas for their extemporaneous compounding should not be included in the N. F.

One advantage in the use of low alcohol elixirs is the saving in alcohol. It may be estimated that such a saving in the United States would be not less than one million gallons per year, if the proposed changes were accepted.

The great advantage of such simple dosage relation of medicated elixirs to both prescriber and dispenser are so obvious that further comment here seems hardly necessary. Every step toward placing the art of pharmacy on a scientific basis may be considered a step forward. The scientific dosage of elixirs would seem to be such a step.

#### DISCUSSION.

In the discussion that followed, A. H. Clark inquired as to the keeping quality of sodium bromide in elixirs; also whether salicylates or benzoates might be used for their preservative power. The question also came up as to the use of saccharin in place of sugar. Dr. Fantus replied that there was no doubt that certain medicaments in elixir did have preservative power; and that salicylate or benzoate were generally not required and perhaps not desirable in view of popular prejudice against them. He also spoke of the popular prejudice against saccharin; but, as it no doubt is harmless, it should be used whenever pharmacutic necessity requires it. A saccharin sweetened elixir would also meet the requirements for a sweet vehicle for medicines of diabetics. Saccharin is properly considered an adulteration in foods when used in place of sugar, as it has no food value.

E. L. Newcomb inquired about frequent doses of elixir, and mentioned an instance in his own family where elixir of potassium acetate had been prescribed every fifteen minutes until the desired therapeutic result was obtained. Dr. Fantus stated that the question of broken dosage is a matter of policy. It is most commonly desirable to give doses as rarely as possible.

Dr. McGuigan inquired for the reason of both iron phosphate elixirs in the N. F. Dr. Fantus replied that N. F. scope is governed by a different principle than the U. S. P. The N. F. committee has no sense of responsibility regarding therapeutics. Admission is based entirely on the use of the preparation. Incidentally he mentioned that the only medicated elixir adopted for the U. S. P., that of benzyl benzoate, seems in danger of being almost obsolete by the time the Pharmacopœia is published.

In reply to an inquiry as to the alcohol in elixir of cascara sagrada, Chairman Cook stated that the fluidextract of cascara contained 20% of alcohol, and so does the aromatic elixir with which it is mixed.

C. M. Snow, in commenting upon the paper, stated that in the experimentation the alcohol was kept down just as low as possible; and that this many times resulted in decided improvement of the elixir. Thus, as a vehicle for pepsin, the elixir of almond makes a real cherry phosphate flavored and very palatable preparation. The formula at present proposed, the manufacturers say, will not stand up under all climatic conditions. However, we have not been able to ferment such an elixir with yeast or bacteria. A great advantage in this vehicle is that the small amount of alcohol present does not in any way influence the activity of the pepsin.

A. H. Clark inquired whether oil of cinnamon in elixir might not prove an excellent preservative. He found that it did so in flour paste.

E. N. Gathercoal stated that in one of the exhibits which has been prepared for this conference—a demonstration of the fermentation of low alcohol N. F. elixirs—aqueous elixir of licorice, compound elixir of almond, and elixir of pepsin after the proposed formula, and elixir of cardamom compound were in no way fermented by yeast or bacteria, even when kept in the incubator for days after inoculation. However, all have grown mold excepting the elixir of almond and that did not grow mold after repeated inoculation.

The following recommendation was offered by Dr. Newcomb and unanimously approved by the conference: "It is recommended that every teaspoonful of each simple medicated N. F. elixir should carry an official average dose of the medicament, provided it is practicable, and that each elixir should be considered by itself."

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### SAFEGUARDING AMERICAN PHARMACY.\*

BY SAMUEL C. HENRY.

While all the subjects of the program of the Section on Commercial Interests are of importance and value for the drug business they will not bring the desired results unless certain safeguards are thrown about pharmacy. I do not agree with some of my good friends, that pharmacy is not making progress. I ask any man in this audience who can look back twenty-five years, to determine in his own mind whether pharmacy has not made very decided progress in those twenty-five years. I submit that the reason pharmacy has made the progress it has is due absolutely to the development of organized pharmaceutical movements in this country. I do not agree with some of my good friends that we should have only one great national organization looking after the interests of pharmacy—in my humble opinion, there is not only plenty of room for two pharmaceutical associations, but there is an absolute necessity for the existence and continuation of those two organizations. Just stop a moment and think—not until a few years ago, really not until the time of the formation of the National Drug Trade Conference, was pharmacy given any consideration in this country; absolutely none. I think the first time we received recognition from the governmental forces at Washington was when the National Drug Trade Conference was formed, and, stepping in, succeeded in putting upon the statute books the Harrison Antinarcotic Law. The National Drug Trade Conference during the years of its existence has done much for the elevation of pharmacy, and for its recognition by the administrative forces as well as the legislative branch of our Government. I call your attention to the fact that the Commissioner of Internal Revenue, the official of the Government next to the Secretary of the Treasury, only recently consulted representatives of pharmacy in its different branches, and constituted from those men a trade advisory committee

\* Parts of an address before Section on Commercial Interests, A. Ph. A., Asheville meeting, 1923.