AROMATIC ELIXIR.

Compound Spirit of Orange, soluble	16 cc.
Syrup	375 cc.
Alcohol	250 cc.
Distilled water	380 cc.
To make about	1000 cc.

Mix the soluble compound spirit of orange with the alcohol. Add the syrup in small portions, mixing well after each addition; then in like manner add the distilled water. (The product at this stage is full of minute bubbles, but clears in a few minutes.)

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(5) "The Volatile Oils, Gildemeister and Hoffmann," 2nd Edition by E. Gildemeister, translated by Edward Kremers.
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A STUDY OF VEHICLES FOR MEDICINES.*

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

III. ELIXIR OF PHENOBARBITAL.

If the slogan "Every N. F. preparation a pharmaceutic masterpiece" be adopted, it ought to add immeasurably to the prestige and popularity of its formulas with the medical profession. It may take quite some time to rectify the errors of omission in this respect in the old formulas of this Book, many of which, all will agree, could be improved. We should, however, scrutinize all new formulas that seek admission to this publication from that standpoint. Without pretending to crown the formula we are about to propose as "a masterpiece;"—it is not for us to pronounce it as such—we would like to submit it in competition with other formulas for consideration, most especially, from the standpoint of palatability.

The principle underlying the elaboration of this formula is best illustrated by the following experiment:

1. 0.030 Gm. of Phenobarbital dissolved in 15 cc. of alcohol (95%).
2. 0.030 Gm. of Phenobarbital dissolved in 15 cc. of dilute alcohol (50%).
3. 0.030 Gm. of Phenobarbital dissolved in 15 cc. of 25% alcohol.

It will be found that the taste of Solution 3 is much more bitter than that of Solutions 2 and 1. Of course, Solution 1 is unpleasantly strong in alcohol; and, therefore, one does not hesitate in deciding that Solution 2 gives the best result. The reason for the lower degree of bitterness of the stronger alcoholic solution over the weaker, evidently lies in the physical fact that *a substance will not exchange a good solvent for a poor solvent.* Inasmuch as phenobarbital is so much more soluble

* From the Laboratory of Pharmacology of the University of Illinois.

alcohol than in water, the 50% alcohol is a much better solvent than is the 25% alcohol: and the saliva-saturated mucosa of the tongue and palate is a still poorer solvent. If one desires to test in this case, the validity of the proposition that "*the best solvent is the best vehicle*" all one needs to do is to dilute the solution resulting from Experiment 2 with water, which immediately brings out a great bitterness. Therefore, when the dose is given in this way, it should not be diluted with water.

We secured a rather "delicious" preparation, tasting more like a "liqueur" than medicine, by dissolving a 0.015 Gm. dose of phenobarbital per teaspoonful of 2 parts of "aqueous elixir" to 1 part of "alcoholic elixir." This mixture of solvent would carry even 0.03 Gm. per teaspoonful; but the resulting solution becomes quite bitter. It might be prepared extemporaneously by dissolving the active agent in a mixture of aqueous and alcoholic elixirs, the formulas for which have been previously submitted (article II of this series). It might seem best, however, to present the following formula for its direct preparation:

ELIXIR PHENOBARBITAL.

Elixir of Phenobarbital.

Elix. Phenobarb.

Phenobarbital	**3.75 Gm.**
Gluside	**1.5 Gm.**
Compound Spirit of Orange	**7.0 cc.**
Alcohol	**300 0 cc.**
Glycerin	**200.0 cc.**
Water	**410.0 cc.**
Sucrose	**170.0 Gm.**
Tincture of Cudbear	**6.0 cc.**

Add the compound spirit of orange to the previously mixed solvents. Agitate and permit to stand for 24 hours, with occasional agitation. Filter through a hard filter and dissolve the phenobarbital, gluside and tincture of cudbear in the filtrate; and finally the sucrose, either by solution or percolation and add enough of the mixed solvents to make the product measure 1000 cc.

CONCLUSIONS.

1. An elixir of phenobarbital should be of rather high alcoholic strength, approximately 30%.

2. The dose should not be diluted before taking, as dilution brings out the bitterness.

3. A formula is offered for comparison with others submitted.

4. If the formula be adopted, it might be prepared either directly as stated, or else indirectly by dissolving the required dose in a mixture of 2 parts of the "aqueous" to 1 part of the "alcoholic elixir," the formulas for which have been previously submitted.

IV. ELIXIR OF AMIDOPYRINE.

In constructing a formula for an Elixir of Amidopyrine that might be as palatable as possible, we have tried the following vehicles, dissolving 0.150 Gm. ($2^1/_2$ gr.) of amidopyrine per teaspoonful, which is one-half of the official average dose:

Aromatic Elixir
Iso-alcoholic Elixir, 50%
Compound Elixir of Taraxacum
Elixir of Glycyrrhiza
Elixir Bitter Almond Comp.—made with 50% alcohol
An Alkaline Elixir of Eriodictyon—made with 50% alcohol
Syrup of Glycyrrhiza
Aromatic Syrup of Eriodictyon

In comparing the tastes of these preparations it seems evident to us that the alcoholic vehicles are better than the aqueous vehicles, and that the stronger alcoholic vehicles are superior to those weaker in alcohol. This is as might be expected from the fact that the amidopyrine is much more soluble in alcohol than in water; and it might serve as another illustration of the proposition that "the best solvent is the best vehicle."

In comparing elixirs of analogous alcohol concentration, we find that an alkaline elixir of eriodictyon made with 50% alcohol provides by far the best disguise, subduing the bitterness to a greater extent than any of the others. That this is not merely due to solvent power is evidenced from the fact that the bitterness is not brought out by dilution, as does occur when the previously proposed Elixir of Phenobarbital (4th Communication) is diluted with water. It must, therefore, be due to specific adsorption of the amidopyrine by the eriodictyon resin.

We have proof, by test-tube experiments, that such adsorption actually occurs. When we add 1 cc. of fluidextract of eriodictyon to portions of 5 cc. and 10 cc. of a solution of 1:1000 of amidopyrine, we obtain a colloidal precipitate which is very difficult to remove from the liquid. After clarification with dilute sulphuric acid, it is readily demonstrated by means of Mayer's Reagent that about nine-tenths of the amidopyrine has been taken out of solution. We therefore know that eriodictyon resin combines with amidopyrine. That this combination will be active in the system is made evident by the fact that the precipitate dissolves in $N/100$ HCl, which is about one-fifth the hydrochloric acid strength of the average gastric juice.

We, therefore, respectfully submit the following formula for consideration for possible admission to the National Formulary:

ELIXIR AMIDOPYRINÆ.

Elixir of Amidopyrine.

Elix. Amidopyrin.

Oil of Bitter Almond	**0.5 cc.**
Vanillin	**1.0 Gm.**
Gluside	**1.5 Gm.**
Amidopyrine	**37.5 Gm.**
Fluidextract of Eriodictyon	**30.0 cc.**
Solution of Potassium Hydroxide	**27.5 cc.**
Alcohol	**500.0 cc.**
Syrup	**350.0 cc.**
Orange Flower Water, a sufficient quantity,	
To make	**1000.0 cc.**

Dissolve the oil of bitter almond, the vanillin and the gluside in the alcohol, then add the syrup. Mix. Dissolve the amidopyrine in the above solution.

Mix the fluidextract of eriodictyon and the potassium hydroxide solution; add it to the amidopyrine solution and mix. Finally add enough orange flower water to make 1000 cc.

The above given formula has been constructed with the N. F. Elixir of Bitter Almond as a basis, this having been selected because bitter almond is in itself a good disguise for the bitter taste. We have fortified the elixir by the addition of fluidextract of eriodictyon because of its power of disguising alkaloids and similar bodies, such as amidopyrine. The quantity of fluidextract of eriodictyon has been chosen at the maximum that will still be pleasant. A greater proportion would develop the inherently unpleasant taste of the yerba santa to an offensive degree. The addition of the potassium hydroxide is necessary to secure a clear solution.

We believe that an elixir of the composition elaborated for the disguise of the amidopyrine might also be useful for other similar medicines. We, therefore, would like to submit the following formula for consideration as a possibly useful strongly alcoholic vehicle for alkaloids:

ELIXIR ERIODICTYI ALKALINUM.

Alkaline Elixir of Eriodictyon.

Elix. Eriodict. Alkal.

Oil of Bitter Almond	**0.5 cc.**
Vanillin	**1.0 Gm.**
Gluside	**1.5 Gm.**
Fluidextract of Eriodictyon	**30.0 cc.**
Solution of Potassium Hydroxide	**27.5 cc.**
Alcohol	**500.0 cc.**
Syrup	**350.0 cc.**
Orange Flower Water, a sufficient quantity,	
To make	**1000.0 cc.**

Dissolve the oil of bitter almond, the vanillin and the gluside in the alcohol, then add the syrup. Mix.

Mix the fluidextract of eriodictyon and the potassium hydroxide solution and add to the above solution. Finally, add enough orange flower water to make 1000 cc.

In suggesting the desirability of introducing this elixir of eriodictyon, we would like to point out that we have not reversed our opinion regarding the desirability of deleting the now official elixir. We recommend this deletion because the "Aromatic Elixir of Eriodictyon" is practically not prescribed at all. It is a most unstable preparation in that it precipitates continually. It is an irrational preparation in that a considerable and undeterminable proportion of the active disguising principle of eriodictyon, the resin, is unceremoniously filtered out. It also suffers from a redundancy of ingredients, containing as many as thirteen, several of them without any good and sufficient reason or advantage. We found that the official elixir contains neither enough alcohol nor of the resin of eriodictyon to give nearly as satisfactory a result in disguising of amidopyrine as the above

proposed elixir, for which the name "Alkaline Elixir of Eriodictyon" might be suggested in order to distinguish it from the elixir at present official.

CONCLUSIONS.

1. An elixir of amidopyrine should be a strongly alcoholic elixir, about 50%, because amidopyrine is more soluble in alcohol than in water.

2. The presence of eriodictyon resin in alkaline solution greatly increases, by adsorption of the amidopyrine, the disguising power of an elixir intended to carry it.

3. An elixir of eriodictyon which serves so admirably as a vehicle for this alkaloid-like body, might also be useful as a vehicle for other similar agents; and its consideration for possible inclusion in the National Formulary, under the title "Alkaline Elixir of Eriodictyon," is suggested.

THE NEW YORK STATE PHARMACY SYLLABUS.*

BY C. W. BALLARD, PHAR.D., PH.D.

The Pharmacy Law of New York State provides for the granting of four degrees in pharmacy. The graduate in pharmacy, Ph.G., is conferred upon the completion of a three-year course with a minimum of 750 hours yearly; the pharmaceutical chemist, Ph.Ch., a three-year course of 1000 hours yearly; the bachelor of science in pharmacy, B.S.Phar., was originally a four-year course of 1000 hours yearly but is now on a semester-hour basis with a minimum of 3600 clock hours; the doctor of pharmacy, Phar.D., representing two years of graduate study subsequent to the attainment of the bachelor's degree. Graduates of both three-year courses are eligible for licensing before the Board of Pharmacy.

The recently issued Pharmaceutical Syllabus IV contemplates a four-year course and is manifestly not applicable to a course of three years' duration. In view of this situation the New York State Education Department has prepared a three-year schedule and syllabus which represents a modification of the Pharmaceutical Syllabus IV. The four-year course, in operation for several years in New York State, is retained and the National Syllabus might have been adopted for this course if it had fulfilled the requirements of the Education Department for the bachelor's degree. The specifications adopted for this four-year course may be briefly stated as follows: 1. It must include all the subjects and hour allotments of the three-year course; 2. It must include a minimum of 3600 clock hours instruction over four calendar years; 3. The division of subjects shall approximately represent fifty per cent each of professional and nonprofessional work; 4. The course shall extend over five days weekly in each calendar year. These requirements, especially the second, necessitated the preparation of a statement of the hours and subjects to be required in both the three- and four-year courses. This syllabus

* Section on Education and Legislation, A. PH. A., Madison meeting, 1933.