

A STUDY OF VEHICLES FOR MEDICINES.

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ISO-ALCOHOLIC ELIXIRS.

It is now thirteen years (4) since the idea of "iso-alcoholic elixir" was brought forward. By this term is meant an elixir of an alcoholic strength just sufficient to dissolve the medicament for which the elixir is to serve as a vehicle. To accomplish this, we require two basic elixirs: 1, an *aqueous elixir* containing a minimal percentage of alcohol and an *alcoholic elixir* containing a high percentage of alcohol. These two have to be mixable in all possible proportions. The advantage of using the term "iso-alcoholic elixir" (5) in prescribing, lies in the fact that it is practically impossible for the physician to remember the exact alcoholic strength required for dissolving all the various drugs he prescribes. It would surely be a great comfort to him, could he, by employing this designation, feel assured that the pharmacist would always deliver a perfectly clear and compatible preparation. This the pharmacist could readily do, possibly with the aid of his reference books, if he had the two basic elixirs in stock. What happens when aromatic elixir is used instead of iso-alcoholic elixir is shown by the following experiments:

EXPERIMENTS.

1. Tincture of digitalis 0.5 cc. mixed with enough aromatic elixir to make a teaspoonful gives a copious precipitate. The same dose added to a mixture of alcoholic elixir 3 parts, aqueous elixir 1 part—the proportions of alcohol and water used in the menstruum—is, of course, perfectly clear.
2. Tincture of veratrum viride, 0.5 cc. added to aromatic elixir 4 cc., precipitates even more copiously than does the digitalis mixture. Using the alcoholic elixir, which is required by the strongly alcoholic menstruum employed in the extraction of the drug, yields a perfectly clear and safe preparation.
3. Tincture of aconite 0.3 cc. whose menstruum is alcohol 7 parts, water 3 parts, precipitates with the official aromatic elixir 4 cc.; but naturally does not, when added to iso-alcoholic elixir made in the proportions of alcoholic elixir 7, and aqueous elixir 3.
4. Tincture nux vomica 0.5 cc. plus aromatic elixir 4 cc. is cloudy. The same dose added to the proper mixture of alcoholic and aqueous elixirs, 3 to 1, remains clear.
5. Tincture colchicum seed, 2 cc., added to aromatic elixir, throws down a few flocculi. Using alcoholic elixir 3, and aqueous elixir 2, gives a clear preparation.
6. Tincture lobelia, 1 cc. added to a mixture of equal parts of aqueous and alcoholic elixirs remains clear, while a precipitate forms with the aromatic elixir.
7. Fluidextract of buchu, 2 cc. added to aromatic elixir yields a copious precipitate, while a clear solution results when the dose is added to the alcoholic elixir.
8. The same is true when a dose of 0.1 cc. of fluidextract of cannabis indica is added to aromatic elixir, while the alcoholic elixir yields a clear solution.

In all these experiments, the average pharmacopœial dose was added to enough elixir to make a teaspoonful. The turbidity resulting in all of these cases with the aromatic elixir of the U. S. P. is not only unsightly but introduces, in some of these instances, an element of danger, as many of these precipitates are toxic. Insufficient shaking of the bottle before taking would lead to a possibly dangerous inequality of dosage. In those preparations, on the other hand, in which the iso-alcoholic elixir was used, a perfectly clear preparation results.

In case of chemicals, the term iso-alcoholic elixir would obviously mean that mixture of aqueous or alcoholic elixir, or either of them alone, that would give a clear solution with the minimal percentage of alcohol.

Thus, for instance, a physician who might want to prescribe the average Pharmacopœial dose of sodium bromide (1 Gm.) in elixir; and who doubted, as he should, that this quantity would dissolve in aromatic elixir, might prescribe it with iso-alcoholic elixir as the vehicle. The pharmacist, knowing that this salt dissolves much more readily in water than in alcohol, would employ the aqueous elixir for its solution. The U. S. P. aromatic elixir does not dissolve more than 0.60 Gm. (10 gr.) of sodium bromide per teaspoonful.

The use of the term "iso-alcoholic elixir" by the prescriber and the proper interpretation of it, by the pharmacist, would avoid the interesting incompatibility arising, when the physician prescribes chloral and bromide dissolved in elixir. In the aqueous elixir it is perfectly compatible. The same doses dissolved in the official elixir, results in the "salting out" of chloral alcoholate. If the attempt is made to dissolve the chloral and bromide in the alcoholic elixir, a great excess of sodium bromide remains undissolved.

A physician who might desire to prescribe an average official dose of terpin hydrate (0.25 Gm.) in solution, need not worry about its solubility, if he specifies iso-alcoholic elixir as the solvent. The pharmacist would dissolve this dose in the alcoholic elixir, and thus secure a perfect solution of an active dose of terpin hydrate. Parenthetically, be it remarked, that the dose of the terpin hydrate in the N. F. elixir of terpin hydrate is merely 0.087 Gm., approximately $1\frac{1}{2}$ grains, which is a rather small dose.

Professor Langenhan, having found that the two elixirs for the preparation of iso-alcoholic elixir, as previously elaborated, produced a turbidity in those dilutions in which the aqueous elixir strongly predominated (under certain temperature conditions), it was found desirable to increase the alcoholic strength of the "aqueous" elixir, to approximately 10 per cent of alcohol. This increase in the alcoholic strength might also improve its keeping qualities, which ought to be excellent in view of the fact that the preparation is now quite saturated with sugar. Our revised formula, therefore, would be as follows:

ELIXIR AQUOSUM.

Aqueous Elixir.

Elix. Aqu.

Compound Spirit of Orange.....	10.0 cc.
Alcohol.....	100.0 cc.
Glycerin.....	200.0 cc.
Sucrose.....	320.0 cc.
Distilled Water, a sufficient quantity,	
To make.....	1000.0 cc.

Mix the alcohol, glycerin and water, and add to them the compound spirit of orange, agitating thoroughly from time to time, and permit to stand twenty-four hours. Filter through a hard filter (Whatman 50) returning, if necessary, the first portions of the filtrate until it passes through clear. Dissolve the sucrose in the filtrate by agitation or percolation, and add enough of the solvent mixture to make the product measure 1000 cc.

ELIXIR ALCOHOLICUM.

Alcoholic Elixir.

Elix. Alc.

Compound Spirit of Orange.....	4.0 cc.
Gluside.....	3.0 Gm.
Glycerin.....	200.0 cc.
Alcohol, a sufficient quantity,	

To make..... 1000.0 cc.

Dissolve the compound spirit of orange and the gluside in the alcohol, add the glycerin and sufficient alcohol to make the product measure 1000 cc. and filter.

ELIXIR ISO-ALCOHOLICUM.

Iso-Alcoholic Elixir.

Elix. Iso-Alc.

Aqueous Elixir.....	a certain proportion
Alcoholic Elixir.....	a certain proportion
Mix them.	

Iso-alcoholic elixir is intended to serve as a general vehicle for various medicaments that require solvents of different alcoholic strengths. When, therefore, iso-alcoholic elixir is specified in a prescription, that proportion of its two ingredients is to be used that will produce a perfect solution.

For liquid galenicals, the strength of iso-alcoholic elixir to be used is the same as that of the menstruum or solvent employed in the preparation of the galenical.

When galenicals of different alcoholic strengths are used in the same prescription, the iso-alcoholic elixir to be used is to be of such strength as to secure the best solution possible under the circumstances. This will generally be found to be the average of the alcoholic strength of the several ingredients.

For non-extractive substances, the lowest alcoholic strength of iso-alcoholic elixir should be chosen that will yield a perfect solution. For substances that are readily soluble in water and less soluble in alcohol, the aqueous elixir is to be used. For substances that are readily soluble in alcohol and insoluble in water, the alcoholic elixir is to be employed.

TABLE FOR ADJUSTMENT OF ALCOHOLIC STRENGTH OF ISO-ALCOHOLIC ELIXIR.

Aqueous Elixir.	Alcoholic Elixir.	Suitable as Vehicle for Preparations Requiring the Following Alcoholic Strengths:
Aqueous Elixir		0-10%
4 parts	1 part	10-20%
3 parts	1 part	20-30%
2 parts	1 part	30-40%
1 part	1 part	40-50%
1 part	2 parts	50-60%
1 part	3 parts	60-70%
1 part	4 parts	70-80%
Alcoholic Elixir		80-95%

A comparison of the two above given formulas will show the apparent incongruity that there is a great deal more of the compound spirit of orange in the aqueous than in the alcoholic elixir. This may seem all wrong, in view of the fact that much more of the compound spirit of orange will dissolve in the alcoholic

than in the aqueous elixir. In point of fact, however, it is not necessary to add more than the 0.4% of the compound spirit of orange as suggested in the formula for the alcoholic elixir, to make it fully as strongly flavored as the aromatic elixir which no doubt contains, when cleared of the excess of oil, even a smaller percentage than that. The only justification for using so large a proportion of the compound spirit of orange in the preparation of the aqueous elixir lies in the observation we made that this larger proportion produces a more fully flavored elixir than any smaller proportion would. It seemed as well flavored as if we had used the more water-soluble "terpeneless" oil of orange. As the expense of this latter quality of the oil of orange is prohibitively great, we believe that we are dissolving out some of this portion from the large excess of the oil of orange we are using; and it is cheaper to waste the rest than to insist upon the terpeneless oil.

Incidentally, it might be noted that the alcoholic elixir, as it contains no sugar, might be used as a pleasant vehicle for medicaments intended for the diabetic, in whom the sugar-containing aromatic elixir would be contraindicated.

CONCLUSIONS.

1. The present formula for the preparation of aromatic elixir is very time-consuming.

2. To lessen the time required, the following modifications of the official formula are proposed: (a) lessen the viscosity by dissolving the sugar after clarification; (b) dispense with the necessity of using talcum by securing dispersion of the oil mixture in droplets large enough to be intercepted by a hard filter; (c) by permitting the mixture to stand for some time with occasional agitation before filtration, saturation of the solvent can, no doubt, be secured even by the larger droplets. A formula embodying these principles is submitted.

3. Formulas are advanced for an "aqueous elixir" and an "alcoholic elixir," which are mixable with each other in all proportions. The official recognition of these elixirs would make it possible for the physician to prescribe "iso-alcoholic elixir," meaning by the term an elixir of the *same* alcoholic strength as the menstruum of the galenic preparation for which it is to serve as vehicle.

REFERENCES.

- (1) Silver, *Practical Druggist*, 48 (1930), 37.
- (2) Schiffler, *Ibid.*, 48 (1930), 17.
- (3) Krantz and Carr, "Further Studies in Filtration," *JOUR. A. PH. A.*, 21 (1931), 785.
- (4) B. Fantus, *Ibid.*, 9 (1920), 708.
- (5) B. Fantus and C. M. Snow, *Ibid.*, 10 (1921), 277.

IVY POISONING.

The Ohio State Division of Conservation is advocating the use of a 5 per cent solution of potassium permanganate as a first aid or emergency treatment for ivy poisoning, in response to many inquiries from anglers and campers. It should be applied by swabbing with cotton or soft cloth. This treatment is recommended by Dr. J. F. Couch of the U. S. Department of Agriculture.

The Division also broadcasts the information

that ivy poisoning can be prevented in many cases by using the following wash, devised by Dr. J. B. McNair of Field Museum, Chicago: 5 per cent solution of ferric chloride in a 50-50 mixture of water and glycerin. Before going out, wash the exposed part of the skin and allow the solution to dry before subjecting the exposed parts to possibility of infection. The iron in the mixture combines with the poisonous element in the ivy and changes it into a harmless, non-poisonous compound.