

The protection of labels as described, making them washable and durable, is not a frill which can just as well be omitted, but represents, rather, a technique which should be used in every retail and hospital pharmacy. In the hospital pharmacy, much time will be saved, since it will not be necessary to replace labels so frequently. The permanence and greatly extended period of legibility of such labels will prevent accidents and save lives. We need only recall the recent tragedy in an Australian hospital, where the life of a patient was lost because a young nurse administered belladonna instead of syrup of figs. The report of the case (1) states that "both were ordinary white glass bottles, and the labels were stained and almost illegible."

There is no reason why pharmacists should not take pride in sending out prescriptions with labels which are not only legible when they leave the store, but which are so durable and washable that they will remain legible a long time afterward.

REFERENCE.

- (1) *JOUR. A. PH. A.*, 21 (1932), 822.

GAINESVILLE, FLA.

A STUDY OF AROMATIC ELIXIR.*

BY C. O. LEE AND MARSHALL CLOSE.¹

An elixir, similar in formula to the present official aromatic elixir was made official in the U. S. Pharmacopœia VI, with the title, Elixir Aurantii. The synonym was Simple Elixir. It was made by percolating cotton, which had been soaked with oil of orange. The menstruum used was composed of water 3 parts and alcohol 1 part.

In the U. S. Pharmacopœia VII, this elixir was replaced by Elixir Aromaticum, and the formula considerably modified. Compound spirit of orange took the place of oil of orange of the previous formula and cotton as a filtering agent was replaced by precipitated calcium phosphate. The only change in the formula in the U. S. Pharmacopœia VIII was that purified talc replaced the precipitated calcium phosphate. Aromatic Elixir, in title, formula and process of making, has remained unchanged through the revisions of the Pharmacopœia since the Eighth.

This fact should not be taken to mean that the formula is, in all respects, wholly satisfactory. A review of the literature reveals that an endless number of complaints have been made about it, mainly, because it consumes so much time in filtering, while others are, that it is too sweet and its alcoholic content too high for certain uses as a vehicle.

Like many of the workers who have preceded us in the study of this preparation, we have sought to acquaint ourselves with the problem, with the hopes of being able to suggest an improved formula. To this end our study presents a review of the literature, under the following headings:

* Section on Practical Pharmacy and Dispensing, Madison meeting, 1933.

¹ Instructor in Pharmacy, Ohio Northern University, Ada, Ohio, Graduate Student, School of Pharmacy, Purdue University Summer Sessions 1931 and 1933.

1. Flavoring Substances.
2. Alcohol and Sugar Content.
3. Clarifying Agents and Methods of Making.

A summary of our studies and recommendations is also given.

THE FLAVORING AGENTS USED IN AROMATIC ELIXIR.

In 1871 (1) the Newark Pharmaceutical Association proposed the following formula for aromatic elixir:

Cort. Aurantii	4 drachms
Sem. Coriand.	2 drachms
Sem. Angelicæ	2 $\frac{1}{2}$ drachms
Cocii Cacti	1 drachm
Spt. Vini Deod.	12 ounces
Aquæ	10 ounces
Glycerinæ	5 ounces
Syrupi	5 ounces

Directions were given to percolate 2 pints. This, it was stated, "is a pleasant vehicle for administering nauseous remedies." In the 1871 Report of the Committee on Unofficial Formulas of the AMERICAN PHARMACEUTICAL ASSOCIATION (2) a formula for simple elixir was recommended in which oils of anise, caraway, cinnamon and fennel were the chief sources of flavor. In 1872 Eberback (3) percolated fresh orange peel, powdered star anise, and cardamon with equal parts of alcohol and water. To this percolate syrup, caramel and the proper amount of water were added. Hancock (4), in 1873, reported that a most satisfactory simple elixir could be made from spirit of orange. Markoe, at the same time, expressed a preference for the tincture made from the fresh orange peel. Later, Hancock (5) proposed a formula which contained spirit of orange and cinnamon water as the flavoring agents. About the same time Remington (6) objected to the use of oils for making the elixir and suggested a formula composed of orange water, cologne spirit and syrup, with Spiritus Vini Gallici as optional for the preparation.

In 1875 the Committee on Formulas for Elixirs of the AMERICAN PHARMACEUTICAL ASSOCIATION (7), reported a formula for simple elixir that contained spirits of orange and cinnamon. Maddox (8), in 1880, suggested the use of oils of lemon, cassia and caraway, in a simple elixir which he considered superior to any he had used.

The United States Pharmacopœia VI contained a formula for Elixir Aurantii (simple elixir) with oil of orange as the only flavor. "The New York and Brooklyn Formulary of Unofficial Preparations" (11) proposed a formula for Aromatic Elixir, in which Aromatic Spirit was the flavoring agent. Aromatic spirit was an alcoholic solution of the extractive principles of fresh orange and lemon peel, bruised coriander and oil of star anise. The same formula, together with four others, was proposed in "A Preliminary Draft of a National Formulary" (12). The second of these formulas was composed of solutions of the oils of orange, cinnamon, anise, bitter almond and tincture of cardamon. The third contained only oil of orange and orange flower water. The fourth contained the tinctures of fresh orange and lemon peel and orange flower water. The fifth was made by percolating cinnamon, nutmeg, cassia, cloves, myrrh and aloe with the addition of a small amount of orange flower water.

Elixir Aromaticum U. S. Pharmacopœia VII contained compound spirit of orange as the flavoring agent. In 1896, Ott (14) suggested that the elixir should be made from the oils rather than from the compound spirit of orange. McIntyre pointed out that the use of the compound spirit of orange was a means of assuring greater accuracy in measuring small quantities of the oils and that the spirit would keep better than the oils, so far as flavor was concerned. In 1902, Bradford (16) suggested the use of tincture of sweet orange. Scoville (19), two years later, proposed a formula, which, he said, corresponded to the official product in character and strength but was an improvement in vigor and delicacy. He suggested the use of the tinctures of fresh orange and lemon peel, oil of coriander and white wine. Johnson (25), however, after considerable experimentation, decided that the official formula containing compound spirit of orange could hardly be improved upon as a flavor. In 1912, Egan (29) said that the aroma and flavor of the

official elixir could be greatly improved by dissolving the compound spirit of orange in the alcohol and allowing the solution to remain in a refrigerator for 48 hours. The *Druggists Circular* (34) printed a formula in which soluble orange was used. The editor pointed out, however, that such flavors were looked upon with suspicion. Beringer (39) suggested the addition of 20 cc. of oil of cinnamon to each liter of the compound spirit of orange for this elixir. Jones (41) suggested the use of terpenless oils of orange and lemon together with anethol and oil of coriander in a concentrated soluble formula, 30 cc. of which, when properly diluted with alcohol, syrup and water, made a good simple elixir.

THE ALCOHOL AND SUGAR CONTENT OF AROMATIC ELIXIR.

Aromatic elixir seems to have been used as a vehicle for a number of years before there was much question as to its sugar and alcohol content. In 1902, Bradford (16) suggested an improved formula in which glycerin represented 25% of the total volume and contained neither sugar nor syrup. Fleet (20) later proposed a similar formula which he termed, *Elixir Aurantii Sine Saccharum*. Heffner (22), in 1906, suggested that care should be exercised in using the official elixir as a vehicle in children's medicines because of its high alcoholic content and because of its incompatibility with certain salts. Johnson (25) also considered the alcohol content too high and after some study of the problem recommended a formula containing about 6.5% by volume of alcohol. Fantus (38) suggested that the alcohol content of this preparation should be adjustable to any desired strength. He proposed a formula containing 5% alcohol, capable of further fortification with alcohol as occasions required. Egan (40) proposed a formula containing about 8% alcohol and approximately 35% by volume of glycerin. He gave, as his reasons for these changes, the prohibition regulations and the scarcity of sugar. He claimed that his formula made a product not only equal in quality to that of the official preparation, but that it was cheaper.

In 1923, Snow and Fantus (42) found objection to the high alcohol content of simple elixir and proposed a formula for an aqueous elixir which contained 5% of alcohol and 20% by volume of glycerin, the latter replacing the alcohol of the official formula. They maintained, also, that their formula was a better solvent for salts that are often prescribed. The *Druggists Circular* (43), in commenting upon non-alcoholic formulas for simple elixir, said that without alcohol it would be lacking one of its principal ingredients. A formula suitable for diabetics was proposed by Snow and Fantus (45) in 1930. It contained gluside 20 Gm., glycerin 200 cc., alcohol 250 cc. and water enough for 1000 cc. This formula, it is suggested, is miscible in all proportions with alcohol and water. The alcohol content may be reduced by diluting it, in which case it would serve as a vehicle for the bromides.

CLARIFYING AGENTS AND METHODS OF MAKING AROMATIC ELIXIR.

The most vexatious problem connected with the manufacture of simple elixir is that of clarification. *Elixir Aromaticum* is widely used as a vehicle, and it is generally acceptable, but there is almost universal complaint as to the time consumed in filtering it. For this reason many workers have suggested numerous ways of speeding up the filtration time for this preparation. To accomplish this without seriously modifying the formula has proved to be no easy task.

In 1873, Hancock (5) used paper pulp as the clarifying agent, saying that it was free from the chemical objections of magnesium carbonate and chalk. Even though the finished elixir was turbid, it could be used for some purposes. In 1880, Maddox (8) used magnesium carbonate to clarify what he called a superior formula. Moore (9) also recommended the use of magnesium carbonate. Simple elixir, U. S. Pharmacopœia VI was made by pouring a solution of alcohol, 1 part, and water, 3 parts, over cotton packed in a percolator which had been wetted with oil of orange. The sugar was dissolved in the percolate and the product strained. "The New York and Brooklyn Formulary of Unofficial Preparations" (11) contained a simple elixir formula which was clarified with phosphate of calcium. In "A Preliminary Draft of a National Formulary" (12) five simple elixir formulas were proposed. For one of these, calcium phosphate was the clarifying agent, for another, carbonate of magnesia and for two others, talcum. *Elixir Aromaticum*, U. S. Pharmacopœia VII was clarified by the use of calcium phosphate. In 1896, Ott (14) used precipitated calcium phosphate in a proposed elixir formula. Talcum appeared in the

formula for Elixir Aromaticum U. S. Pharmacopœia VIII, replacing calcium phosphate in the formula of the previous issue. Parry (15) suggested a formula which, he said, needed no clarifying agent if allowed to stand two weeks before filtering. Dunning (17) saved time in making this elixir by adding the calcium phosphate to the mixture of compound spirit of orange, alcohol and water, in which, after filtering, sugar was dissolved. This avoided the tediousness of filtering a thick syrupy solution. Caldwell (18), in 1903, reported that the preparation could be made to filter clear at once, if mixed in the proper manner. Fleet (20) advised sprinkling the filter paper with calcium phosphate, before filtering, rather than mixing it with the liquids as is usually done. According to Toplis (21), simple elixir is, "one of the greatest time consumers of the U. S. P." He modified the official process by mixing the compound spirit of orange with the talcum. To this was added the solution of alcohol and water, which was filtered after the manner of making official waters. The required amount of sugar was dissolved in this filtrate. Posey (23) speeded the time of making even more by mixing the talc, the compound spirit of orange and the water and then filtering. The syrup and alcohol were then added to the filtrate. Doyle (24), in 1909, used magnesium carbonate as the clarifying agent. The mixture was allowed to stand until a clear supernatant liquid separated which, it is stated, filtered clear in a short time.

In 1910, the *Western Druggist* (27) printed a formula in which it was suggested that the alcohol be added in part to the compound spirit of orange, talc and water and the mixture filtered. The remainder of the alcohol was added to the syrup, which in turn was dissolved in the clear filtrate. Dunn (28), under the title of "Shortcuts and Improvements," suggested that the compound spirit of orange and alcohol be mixed with kaolin and filtered, and that water be added to this filtrate, in which sugar was then dissolved, and the whole filtered through cotton. Five grams of magnesium carbonate, according to Sass (30), gave better results in filtering than did the required amount of talcum. In 1913, Daniel (31) modified the official process for simple elixir somewhat, but said, "It is my opinion that quick and easy, and first class work are incompatibilities." Possehl (32), in 1914, suggested that the official elixir could be improved by first making a water, in the usual way, from the compound spirit of orange and talc, and adding to it the syrup and alcohol. Fried (33), in 1914, said, "one of the easiest preparations to make is aromatic elixir providing a few changes in procedure are made." He suggested that the syrup should be replaced by sugar and added after filtration and then the whole strained, if necessary. Satz (35) filtered the aqueous-compound spirit of orange mixture with talc and to this added the syrup and alcohol. Scher varied this a little. He filtered the compound spirit of orange, alcohol and water mixture with talc and added the syrup to the filtrate. Burge (36) followed Scher's procedure, but used paper pulp as the clarifying medium. Concerning aromatic elixir, Cook (37) said, "It is unfortunate that the purified talc, which is not a satisfactory filtering medium, was not replaced by purified siliceous earth (Kieselguhr), which has been made official." Purified siliceous earth not only speeds the rate of filtering but clarifies the elixir promptly. Egan (40) maintained that the use of purified siliceous earth, as compared to talc, resulted in clearer elixirs. Jones (41) spoke out of much experience with simple elixir when he said, "Its clarification is very trying on one's patience, and the usual result is a cloudy preparation, even after many repeated filtrations." After a study of the effect of various clarifying agents upon "The Hydrogen-Ion Concentration of Aromatic Elixir," Krantz and Carr (44) concluded that normal magnesium carbonate is admirably suited for use as a filtering agent in this preparation, because it filtered rapidly and yielded an almost neutral elixir. In 1930, Shiflett (46) offered a modified procedure quite similar to one reported in 1910 (27). A solution of 150 cc. of alcohol and 300 cc. of water is made. The compound spirit of orange is then triturated with the talc and mixed with 350 cc. of the above alcohol-water solution. After filtering, 375 cc. of syrup are added to the filtrate. To this is added the remaining 100 cc. of alcohol, and then water enough for 1000 cc. It is claimed that this process requires but one-tenth the time of the official procedure. "If there is any discrimination in flavor, it is in favor of this non-official process." Silver (47) found fault with Shiflett's procedure and offered a slightly different one. Burlage (48), in 1932, studied five methods for making simple elixir: 1. The U. S. P. method modified as to the order of mixing; 2. The U. S. P. procedure unmodified; 3. Shiflett's Method; 4. Silver's Method; and 5. The U. S. P. Method, modified by using double the specified amount of talc. As to speed of filtration, he rated the methods of Shiflett and Silver about equal and superior to the present official and proposed modifications.

Fantus, Dyniewicz and Dyniewicz (49), in 1933, criticized several methods and formulas, which have been proposed. They formulated the three following rules for preparing the elixir: 1. The viscosity must be kept low until after clarification. 2. Filtration through talc and other absorbents must be abandoned, because it consumes time and wastes oil. 3. One must avoid precipitating the oil globules so fine that they will pass through a filter paper and, in turn, a longer time for saturation should be allowed. They propose making the elixir by mixing all of the water with the alcohol, adding the compound spirit of orange, and allowing it to stand for 24 hours, being frequently agitated, then filtering through a hard filter, without the use of any absorbent. Lastly dissolve the sugar in the filtrate.

EXPERIMENTAL PART.

In the face of the rather discouraging results of many workers, to speed up the time of filtration of Elixir Aromaticum without the loss of its very acceptable aroma and flavor, we attempted the impossible. It was decided at the outset that the time consumed in filtering the official simple elixir is an item of no mean consideration. Furthermore, it was assumed that it would be rational to sacrifice, if necessary, a part of the flavoring qualities of the present formula, for one slightly less pleasing, if the objections to the present process could be removed. We have tried, in the work we have done, to incorporate the suggestions of other investigations, although not always in agreement with them upon every point.

In an attempt to speed up the process for making aromatic elixir, a series of 14 elixirs were prepared. The U. S. P. X formula and procedure were used as a basis for the several modified formulas. All deviations from the official formula and procedure are noted for each modification. 1000-cc. quantities were prepared in most cases.

THE MODIFICATIONS.

1. Elixir Aromaticum, U. S. P. X. The formula and procedure of the Pharmacopœia were used and followed and are not repeated here.

2. Paper pulp was substituted for purified talc.

3. Washed talc was substituted for the official talc. This was prepared by washing the talc repeatedly with water by decantation for the purpose of removing all of the very fine filterable particles.

4. The compound spirit of orange was mixed with the talc, to this was added, in portions, the syrup, alcohol and water previously mixed. This was allowed to stand 24 hours and filtered in the usual way.

5. Water and sugar were substituted for the syrup.

The compound spirit of orange was dissolved in the alcohol, and water added in portions to make 818 cc. This was mixed with the talc and filtered. The sugar was dissolved in this filtrate and made up to 1000 cc. by the addition of a solution of alcohol 1 and water 3. (This is the method of Toplis *q.v.* (21).)

6. After the method of Scher, *q.v.* (35) the compound spirit of orange, alcohol and water were mixed with the talc and filtered as usual. The syrup was added to the clear filtrate and the quantity made up to 1000 cc. according to the official method.

7. Glycerin, 125 cc., was substituted for an equivalent amount of syrup. The compound spirit of orange, alcohol, water and talc were mixed and filtered, as officially directed. The syrup and glycerin were added to the clear filtrate and the volume made up to 1000 cc. as usual.

8. An elixir was made by saturating the solvents. The alcohol, syrup and water were carefully mixed. Compound spirit of orange was then added dropwise, with shaking after each addition, until the solution became saturated.

9. Number eight was repeated with a slight change in the solvent. 125 cc. of glycerin were used to replace an equivalent amount of syrup. The alcohol, glycerin, syrup and water were then mixed. Compound spirit of orange was then added as in number eight.

10. An elixir was prepared according to the Shiflett formula (46). Dilute 150 cc. alcohol and 300 cc. of distilled water. 350 cc. of this solution were mixed with the mixture of talc and compound spirit of orange, and the whole filtered. The filter was finally washed with the remaining 100 cc. of alcohol and water solution. Syrup was then added to this filtrate, in divided portions with agitation after each addition. The remaining 100 cc. of alcohol was then added and the volume made up with water, if the amount needed was small; with alcohol 1 part and water 3 parts, if the amount needed was large.

11. Sugar and water were substituted for syrup. The compound spirit of orange and talc were mixed. 575 cc. of water were added to this mixture and the whole agitated frequently for 15 minutes and then filtered in the usual way. In 550 cc. of the clear filtrate, 320 Gm. of sugar were dissolved, 250 cc. of alcohol then added and the volume made up to 1000 cc. by addition of the first clear filtrate.

12. The U. S. P. simple elixir was prepared, using purified siliceous earth instead of the talc.

13. The U. S. P. simple elixir was prepared, using kaolin instead of the talc.

14. The U. S. P. simple elixir was prepared using magnesium carbonate instead of the talc.

TABLE I.

Formula No. ¹	Appearance of Finished Product.		Colored.	Times Filtrate Was Returned Before It Cleared. ²	Rank as to Time Required to Prepare. ³	Condition after Two Years. ⁴		
	Clear.	Cloudy.				Odor.	Taste.	Sediment.
1	cl	7	13	g	g	s
2	cl	f	...	22	14	g	g	s
3	cl	4	11	g	g	s
4	cl	5	12	g	g	s
5	2 w	1st	...	4	10	g	g	pro
6	2 w	1st	...	4	8	g	g	s
7	2 w	1st	...	4	9	g	g	pro
8	...	clo	...	nf	5	p	p	oil
9	...	clo	...	nf	6	p	p	oil
10	2 d	1st	...	3	7	t	t	s
11	cl	3	3	g	g	s
12	cl	1	4	g	g	...
13	cl	2	2	g	g	...
14	cl	...	sy	0	1	g	g	...

ABBREVIATIONS: cl, clear; 2 w, after 2 weeks; 2 d, after 2 days; f, faintly; 1st, at first; clo, cloudy; sy, slightly yellow; nf, not filtered; g, good; p, poor; t, terebinthinate; s, slight. pro, pronounced; oil, oil on surface.

¹ See preceding pages for formulas and methods of making.

² Approximately 100-cc. portions were returned each time.

³ Number one required the shortest time, about an hour, and the longest time, about 24 hours. ⁴ Two years' time applies to Nos. 1 to 11; about two months only to Nos. 12, 13 and 14.

Table I gives, in brief, our observations of the fourteen modifications of the simple elixir made as outlined above. They were observed (1) with respect to clearness and color, (2) the number of times that it was necessary to return 100-cc. portions back through the filter before the filtrate became clear; (3) a comparative scale of the speed or time required to complete each product, and (4) condition as to odor, taste and sediment after standing in storage for two years.

The results, as expressed in Table I, verify many of the observations of other workers upon this problem, as for instance the difference in filtering time with talc as compared to purified siliceous earth or magnesium carbonate.

A SIMPLE ELIXIR OF LOW ALCOHOL CONTENT.

We are cognizant of the objections that have been made to making a simple elixir by the so-called "aromatic water" method and also that it has been said that aromatic elixir with little or no alcohol in it is without one of its very important constituents. Even so we chose to experiment with formula Number 11 which has been given. Three lots were made by the "aromatic water" process. These were termed Lots A, B and C and each contained successively smaller percentages of alcohol. Lot A contained 15% alcohol; Lot B, 10% and Lot C, 5%. These three lots kept perfectly for more than six weeks. The only difference in taste that we could detect, was attributed by us to the alcoholic content. We therefore concluded that a reasonably good aromatic elixir, with any desired alcohol strength, is possible.

SIMPLE ELIXIRS AS OTHER ELIXIR VEHICLES.

A. Elixir Glycyrrhizæ U. S. P. X.—Since Elixir Glycyrrhizæ is a preparation composed chiefly of aromatic elixir, five lots of it were prepared using the modified formulas numbered 1, 11, 12, 13 and 14, previously described. These five lots were observed over a period of several weeks. They were, from all appearances, quite alike, even in the slight sedimentation that resulted.

B. Elixir Potassii Bromidi N. F. V.—Approximately 30% Aromatic Elixir is contained in this preparation. Three lots of it were prepared, using elixir modification formulas, numbering 1, 11, and a modification of number 11 containing but 10% alcohol described as Lot B in the paragraph under "A Simple Elixir of Low Alcoholic Content."

These three preparations were made according to the official directions. They were studied over a period of several weeks. No observable differences between them were noted during this time.

These observations, though few in number, do indicate that some of the modified simple elixirs, which have been described, are usable and seem to compare well in that respect with the official elixir which is tedious to prepare and of questionable alcoholic content.

A PROPOSED SIMPLE ELIXIR FORMULA.

As a result of our study of the official simple elixir, especially with respect to

the difficulties of making, as well as to other objections that have been made, the following formula and method are suggested for the preparation of aromatic elixir:

Compound spirit of orange	12 cc.
Purified talc	30 Gm.
Sugar	320 Gm.
Alcohol	The desired amount
Distilled water, to make	1000 cc.

Carefully mix the compound spirit of orange and talc by trituration. Add about 800 cc. of water, in convenient portions, and triturate after each addition. Agitate frequently for about 15 minutes and filter in the usual manner. Dissolve the sugar in 550 cc. of the clear filtrate and to it add the amount of alcohol desired. Finally make up to 1000 cc. with the required amount of the clear filtrate.

CONCLUSIONS.

Although this recommended formula may contain somewhat less of the flavoring principles than does the official elixir, we think it is sufficiently strong in flavor to serve as a good vehicle. We recommend it for the following reasons:

1. The time required to prepare it is approximately one-tenth that necessary for the present official simple elixir.
2. The alcohol strength of this elixir may be varied at will without modifying the technique of making.
3. The preparation is always the same clear product regardless of a variation in the alcoholic content.

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PURDUE UNIVERSITY SCHOOL OF PHARMACY,
LAFAYETTE, INDIANA.

C. LEWIS DIEHL.*

BY JOHN E. KRAMER.

The name Diehl is synonymous with pharmacy, pioneer and progress. C. Lewis Diehl's connection with the first is well known to every one acquainted with the history of American pharmacy. This profession was evidently his very life and being, as attested to by his career.

That he was a pioneer can be seen in a cross section of his advancement through life. Less than fifty years after the Philadelphia College of Pharmacy had been founded in 1821, Mr. Diehl was the founder of the Louisville College of Pharmacy in Louisville, Ky., and was elected and reëlected, successively, president of that institution for eleven years. He proved to be a pioneer as one of the members of the first Board of Pharmacy of Kentucky, retaining that post for twelve years. He opened two drug stores in Louisville, and was one of the pioneers in research work along pharmaceutical lines, being noted for his work on percolation, along with Procter, Squibb and others of his time. Incidentally, this process of extracting the principals of drugs by percolation, developed in America, remained a typical American process, as the European countries never became enthusiastic over the idea, and almost totally ignored it.

Pharmacy, in the time of Diehl, was in an early stage of organization in the south and southwest, and also in the matter of research and the establishing of American pharmaceutical customs. Prof. Diehl was indeed a leader of the pioneers in these fields.

The third synonym is progress. Something once started must be continued, to make it worth while. Professor Diehl applied this idea to pharmacy, for, after

* Section on Historical Pharmacy, A. PH. A., Madison meeting, 1933.