PRACTICAL PHARMACY SECTION

ELIXIRS OF THE NATIONAL FORMULARY.*

BY HORATIO C. WOOD, JR., M.D.[1]

Despite the fact that the National Formulary is a legal standard, in many states on a parity with the United States Pharmacopoeia, it has failed to come into general use by the medical profession. This is unfortunate, because there are in it many excellent formulas which should be valuable additions to the physician's armamentarium. It seems to me, therefore, to be well worth while to inquire into the reasons for this lack of confidence in the book, with the idea that in future editions these faults may be corrected so that it shall receive more popular acceptance. This distrust has been engendered in large part by the fact that the book contains so much that is unworthy of an official standard, that physicians in general have a sort of fear of its reliability. While there are a few things in the Pharmacopoeia which might better be omitted, as a whole that work is so excellent that the medical profession in general have an idea that anything in the Pharmacopoeia must be all right. Certainly they have no such feeling as concerns the National Formulary. This is a great pity, because a widely accepted book of the character of the National Formulary would not only be of large use to the medical profession in illustrating elegant modes of prescribing but would, I believe, serve a useful purpose in lessening the employment of nostrums. Therefore, although the criticisms I am about to offer may seem like disparagement they are really constructive and offered with the hope that in the future the National Formulary may be purged of some of these glaring faults. In order to show how a little blue penciling would have improved the present edition of the National Formulary, I have chosen the elixirs as one of the important vulnerable subjects.

As a whole, doctors do not possess a very extensive knowledge of the subject of properly flavoring their prescriptions. Most of them, however, do know that there is an official aromatic elixir and that it has a rather agreeable taste, and many physicians are prone to employ it almost routinely as a vehicle. They do so, not because of the universal suitability of this elixir, but because of their ignorance of other methods of disguising unpleasant tastes. One would have thought, however, that a committee of such eminent pharmacists as those who have charge of the preparation of the National Formulary would have been able to devise an acceptable substitute which might afford an occasional variant. Out of seventy-six elixirs recognized by the National Formulary, fifty-two contain aromatic elixir, and two others, compound spirit of orange. Nor is the aromatic elixir by any means always the most successful flavor which might have been chosen. I remember well a very interesting paper by Mr. Beringer on the value of vanilla to disguise the taste of bromides, and I presume it was this contribution of Mr. Beringer's which led to the recognition of the compound elixir of vanillin. It seems a strange whimsy of fate, therefore, that not a single one of the elixirs of the bromides contains any vanilla. We have the elixir of ammonium, calcium, lithium, sodium, and potassium bromide, all of them flavored with syrup and aromatic elixir.

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While on the subject of the bromides, attention might be called to the absurd and inconsistent proportions which these elixirs contain. The elixirs of ammonium, calcium, and lithium contain $8^1/_2$ percent of active ingredient. The official dose for the first two of these is given as one fluidrachm, so that the patient would receive five grains of the bromide at a dose, which is a quantity too small to have any appreciable influence. The elixir of lithium bromide contains the same quantity of active ingredient—in fact, when we allow for its lesser atomic weight it contains actually a larger amount of bromide—and yet the dose is given as two fluidrachms. Still more ridiculous in inconsistency is the elixir of sodium bromide, which contains $17^1/_2$ percent as opposed to $8^1/_2$ percent in ammonium bromide and yet is given in twice as large dose.

While on the subject of dosage and to show the total unsuitability of aromatic elixir for some purposes, may I call attention to the elixir of potassium acetate? This contains approximately five grains of potassium acetate in a fluidrachm of aromatic elixir and the average dose is given as four fluidrachms, which represents a reasonable but not excessive amount of the active salt. This amount of potassium acetate is often repeated every two hours, which means that a patient would take in the course of one day an amount of alcohol equivalent to four ounces of whisky. In view of the call being made for conservation of alcohol, this certainly seems a wicked waste of ardent spirits, the more so because potassium acetate is often used in conditions in which alcohol is absolutely harmful.

The editors of the National Formulary prepared two elixirs which were practically free from alcohol and then proceeded not to use them. Lithium salicylate is used practically only in the treatment of gout, in which all physicians are agreed that alcohol is injurious, and yet to get an efficient dose of lithium salicylate in the form of the elixir, the unfortunate patient must ingest the equivalent of nearly half an ounce of whisky with every dose.

A COMPARISON OF THE DOSES OF N. F. ELIXIRS WITH THE U. S. P. AVERAGE DOSES OF THEIR CONSTITUENTS.

	Amount in average dose of N. F. elixir.	U. S. P. average dose.
Elixir Ammonii Bromidi	5.1 grains	15 grains
Elixir Ammonii Valeratis	2.1 grains	8 grains
Elixir Buchu	7.5 grains	30 grains
Elixir Calcii Bromidi	5.1 grains	15 grains
Elixir Calcii Hypophosphitis	4.2 grains	8 grains
Elixir Cascarae Sagradae	30.0 grains	15 grains
Elixir Ferri Phosphatis	2.1 grains	4 grains
Elixir Gentianae	2.1 grains	15 grains
Elixir Guaranae	12.0 grains	30 grains
Elixir Lithii Bromidi	10.2 grains	15 grains
Elixir Lithii Citratis	10.2 grains	8 grains
Elixir Pepsini	1.0 grain	8 grains
Elixir Phosphori	$^1/_{60}$ grain	$^1/_{120}$ grain
Elixir Potassii Acetatis	20.4 grains	15 grains
Elixir Potassii Bromidi	21.0 grains	15 grains
Elixir Sodii Bromidi	21.0 grains	15 grains
Elixir Sodii Hypophosphitis	2.1 grains	15 grains
Elixir Sodii Salicylatis	5.1 grains	15 grains
Elixir Terpini Hydratis	1.0 grains	4 grains
Elixir Viburni Prunifolii	7.5 grains	30 grains

I have thought it might be interesting to compare the quantity of the active ingredients in the officially recommended dose of some of these elixirs with the average dose as given by the United States Pharmacopoeia. I have, therefore, prepared a table showing these comparative doses.

I should like to direct notice especially to the elixir of buchu, containing one-fourth the U. S. P. dose; to the elixir of pepsin, with one-eighth the U. S. P. dose; and, on the other hand, to the elixir of phosphorus with double the pharmacopoeial quantity. The latter is especially objectionable not only because one-sixtieth of a grain of phosphorus is a dangerously large quantity but also on account of the difficulty of reducing the dose.

In looking over the group of elixirs as a whole, one gets the impression that less thought has been expended on many of them than many a doctor would give to a single prescription. For instance, such a thing as the elixir of cascara sagrada, made by simply mixing together equal parts of aromatic fluidextract of cascara sagrada and aromatic elixir seems to me to be an insult to the medical profession as suggesting that they have not intelligence enough to dilute the aromatic fluidextract of cascara sagrada, as well as being far from a triumph of pharmaceutical skill. All such simple combinations as elixir of lithium citrate, of potassium acetate, of the various bromides, of ferric phosphate, etc., might much better be left to extemporaneous prescribing where the doctor could adjust the dose to suit the case at hand.

When we come to study the complex elixirs, those which contain several active ingredients, we begin to tread that dangerous ground of therapeutic efficiency, about which there is much difference of opinion. I am not going to say anything about the advisability, let alone the justifiability, of the use of elixir of hypophosphites, of gentian, of corydalis, or of the formates, except to express my personal opinion that they serve no useful purpose, but I must confess that I stand in amazement at the perfervid imagination which could conceive of a pathological condition where such a conglomeration as the elixir of pepsin, bismuth and strychnine could be indicated. This wonderful concoction contains a trace of the digestive enzyme which is killed by alcohol and murdered by a heavy metal, plus a small quantity of a feeble astringent and an infinitesimal amount of a nerve stimulant.

While talking about pepsin, may I inquire what is the idea of the elixir of pepsin and iron, or of the elixir of cinchona, pepsin and iron? The only possible excuse for the elixir of cinchona alkaloids, iron, bismuth and strychnine is the old idea of "the more the messier." Know ye not, brethren, that pepsin is chemically incompatible with the heavy metals and that alcohol destroys its enzymic activity?

Having called attention to a few of the more glaring faults of these elixirs, I am hearing you wonder whether I have nothing in the way of favorable criticism. Yes, I believe that the elixir of bitter almonds, of anise, of vanillin, of eriodictyon and of gentian deserve recognition as flavoring agents. The elixir of phosphorus may also be of service as affording a pleasant means of exhibiting a drug rather difficult to manage. Perhaps the elixir of iron, quinine and strychnine, of terpin hydrate and of compound glycerophosphates might be continued as concession to those who believe that they possess utility and as being rather difficult for the physician to prescribe extemporaneously. The elixir of sodium bromide, of three bromides, of iron phosphate, of sodium salicylate, and compound elixir of black-

berry, and possibly one or two others might, after some modification, be afforded recognition, but certainly both medicine and pharmacy would be vastly improved by deleting at least sixty of these elixirs as being either unnecessary, useless, or absolutely injurious.

ABSTRACT OF DISCUSSION.

CHARLES H. LAWALL: Dr. Wood's paper contains some very interesting and valuable food for thought and some interesting points are brought out. It must not be forgotten that a large number of preparations are in our U. S. P. and N. F. because the physicians prescribe them and there is a consequent necessity for their standardization.

I remember hearing that a very eminent member of the U. S. P. Revision Committee once said that the basis for admission to the U. S. P. should be the amount of use of a product by physicians and that if there were a sufficiently large number of physicians prescribing brick dust, that article should have standards set for it in the U. S. P. It may be interesting to Dr. Wood, too, to know that the eminent authority credited with the statement was Dr. Horatio C. Wood, Sr.

GEORGE M. BERINGER: There is much in this paper that we can approve and I am thoroughly in accord with many of the statements of Dr. Wood. In my experience in the revisions of the U. S. P. and N. F., I have learned that all revision work is largely made up of compromises and in the Committee on N. F. some of the points here presented were discussed, and while my personal views, for example, as to the proper flavorings for bromide elixirs, were presented, the majority of the Committee were averse to making any change in the flavoring.

Human work is always characterized by some inconsistencies and these inconsistencies and errors as much as the progress of medical sciences necessitate revisions of the standard authorities. When the Federal Food and Drugs Act of 1906 was enacted and specified the tests laid down in the National Formulary as the legal authority for N. F. drugs, we were confronted by a rather anomalous situation as the N. F. laid down no tests, as the N. F. III had been prepared without the thought that it was to be made a legal authority. This necessitated a far more thorough revision of the N. F. than had been previously attempted and it must be admitted that the Fourth Edition is entirely different in character and scientific standing from its predecessors, and further, that it will compare favorably with similar formularies of foreign countries and that it well serves its position as a companion authority with the U. S. P. I fear that we have overlooked that all of such works are the results of evolution and the U. S. P. is now the Ninth Revision while the N. F. is but the Fourth Edition. As such it should be compared with some of the earlier revisions of the U. S. P.

In the National Formulary the pharmacist must, as in other matters, follow the physician and the practice of the medical profession in the United States is responsible for the existence of many of the formulas criticised as therapeutically inactive. While this may be so, the committee on N. F. found that these were so extensively used throughout the country that an official formula was necessary. In a prefatory note the Committee distinctly stated that they were not responsible for the therapeutic value of the formulas presented. Their duty was plainly the making of standards and formulas that were satisfactory from the pharmaceutical standpoint. How well they have discharged this duty is of course open to criticism, but the inclusion of formulas, even though they may be, from the viewpoint of the therapeutic experts, errors are faults of the prescribers of such. Possibly no preparation is more frequently prescribed than is the compound elixir of pepsin or as the N. F. III named it Compound Digestive Elixir. Listening to the demands of the class of the medical profession, the Committee eliminated this formula from the revision with the result that we have now no legal authority or standard for a preparation that is prescribed to the extent of many thousands of gallons and by a number of physician outnumbering many times those who were so strongly objecting to the retention even of the improved formula which had been proposed and which had actually been adopted. My personal strenuous objection did not prevent the Committee reversing itself. But what is the result? Throughout the country, a preparation used to an enormous extent, is being dispensed without any uniformity of color, taste, odor, alcoholic content or enzymic content. The N. F. has failed to discharge, in this respect, the very duty that called it into existence, and, more seriously, a

legal standard has been destroyed and substandard goods to an enormous extent have since flooded the country. Who is responsible for these errors? Are they not really caused by the failure of physicians to agree?

Regarding the formulas for the elixirs, I quite agree that these are entirely too numerous and that medical practice should be so planned as to eliminate a number, but the physicians here again must decide which they will discontinue to use. The formula for Elixir of Cascara Sagrada has been referred to; this well illustrates a principle which held in the N. F., namely to frame formulas wherever possible to permit of extemporaneous preparation. The formula adopted is simply a mixture of fluidextract and elixir. This simplified manipulation can surely not be considered objectionable and the formula appears to have proven satisfactory and has well served its purpose of supplying a standard formula that will insure uniformity in compounding of prescriptions for this article.

Regarding the basic elixirs of the N. F., the committee had in mind two facts, namely the necessity for many medicaments of reducing the alcoholic content of the diluent or vehicle and that, at times, patients became tired of one flavoring and although a combination like the compound spirit of orange was generally liked at times a change was desirable. For these reasons they proposed several new elixirs which widened the list of vehicular flavors so that the physician could select the most appropriate and varying in alcoholic strength from 5 percent or 10 percent up to 30 percent in the curacao elixir. The value of the weaker alcoholic elixirs like the Compound Elixir of Almond, the Compound Elixir of Cardamom and the Compound Elixir of Vanillin is beginning to be appreciated by the physicians and will in time become more popular.

The question of dosage has been raised and the posology of the N. F. has been criticized. With equal force these comments could have been made applicable to the U. S. P. Following the example of the U. S. P., the N. F. has adopted the plan of stating the average doses. Even the word used "*average* dose" was capable of several constructions. Moreover, physicians, whose special function it has been to determine the official statements regarding dosages, could not agree and many inconsistencies exist in the statements of these in both the U. S. P and N. F. As a matter of fact, the doses stated in the National Formulary have been supplied by a physician who has rendered this valuable assistance on a purely medical matter to the N. F. Committee.

J. W. ENGLAND: I believe with Dr. Wood that some of the formulas in the National Formulary are therapeutically illy balanced, but their number is small. The book, as a whole, is the result of years of clinical experience by thousands of successful physicians. Like Topsy, many of the formulas "just growed up." They were originally physicians' prescriptions, gradually acquired a local reputation, and then a national one demanding a standard formula. Originating in various sections of the country, formulas of similar compounds were made of a different content of active ingredient in each dose, but such formulas can be readily standardized in the future, now that the National Formulary is a legal authority with standards that can be enforced.

The extent of the use of a drug or drug preparation is, rightly, the acid test as to whether or not it should be officially recognized. A nationally or widely used drug or drug preparation should have a national standard.

The clinician is the man who should say what drugs and drug preparations should be used in medical practice, and he says this through his prescriptions. No stream can rise higher than its source, and the National Formulary should and does most efficiently represent the wishes of the rank and file of the medical profession in this country.

FRANKLIN M. APPLE: At the meeting of the A. Ph. A., held in Detroit, Mich., in 1914, Mr. Beringer in his address as President of the Association, recommended that an epitome of the N. F. IV be prepared, also that a Committee on Propaganda be created to give a great measure of publicity to the new edition of the N. F., especially so to the members of the medical profession.

It is essential to do so as the medical practitioners judge the N. F. IV by their knowledge concerning the N. F. III, which is freely acknowledged to be far inferior to the N. F. IV, which is a book of legal standards that was prepared to meet such application of it. Unfortunately, the treasury of the A. Ph. A. is not overflowing with funds, hence some other source of funds must be sought to carry out the recommendations of Mr. Beringer, which suggestion was finally passed upon favorably at the Atlantic City, N. J., meeting in 1916. This disposition of the matter

was necessitated by the action taken by the Association at its final session at the Detroit, Mich., meeting, where an apparently diplomatic move to dispose of it was taken, with the result that the Council could not make any move to inaugurate a movement to give the publicity of the N. F. IV that its superiority over the N. F. IV warrants.

Possibly the A. M. A. may have facilities at their command which they will offer upon solicitation of the A. Ph. A. officials, whereby the desired publicity for the N. F. IV can be obtained. I make this suggestion for whatsoever merit it may contain.

PRACTICAL DRUG CONSERVATION.*

BY AMBROSE HUNSBERGER.[1]

The question of conserving drug store supplies during a national war crisis such as the one through which we are passing at the present time would seem to demand the most profound consideration and unflagging persistence of the practicing pharmacist in its solution. It is peculiarly a problem for the pharmacist, inasmuch as he ought to be in the best position to recognize the limitations which will maintain drug conservation within the bounds of common sense without sacrificing efficiency, and he should further be able, by virtue of his practical experience, to determine the line of least resistance to be followed in order that the most helpful results may be achieved in the shortest possible time.

When we stop to consider the close relationship of the pharmacist with the public, we are readily able to recognize his obligation in that direction, and it becomes apparent that whatever he can do in the way of curtailing the communal encroachments involved in the practice of his calling, should be done without the slightest delay. Of course, the thought suggests itself concerning a reciprocal obligation on the part of the public. If it is not a recognized principle now, it will be, probably soon, that many things which are considered indispensable necessities under normal conditions of living, become distinctly non-essentials, if not positive luxuries, during periods of stress and strife. This principle is quite as applicable to the production of drug supplies as to that of any other commodity consumed by the public, and so applied, means relegating to the back top shelf, for the period of the war, many of the "elegant pharmaceuticals" and nostrums, some of which are said to make therapeutic efficiency a secondary consideration at best. What if the tonic elixir does appeal a little less to the eye, nose, and palate, or the cough syrup is only half as cloyey, or the stomachic loses a part of its alcoholic tang, and the favorite digestant temporarily foregoes its emulation of the far-famed cordial of the Benedictine monks—the esthetic must sacrifice itself on the altar of practicability, and it is reasonable to presume that our loyal public will accept its obligation in the matter of conserving drug supplies, which are difficult to secure, when it is made clear that the heaviest demand upon the restricted substances is created by the effort to appeal to its finicky palate.

As regards the problem before us, it may be said that practical conservation in the drug store includes restriction in the use of many articles which under normal conditions are used in enormous quantities without any special thought being given to the availability of future supplies. A brief list (excluding substances employed

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[1] President Philadelphia Branch A. Ph. A., 1917–1918.