THE NATIONAL FORMULARY AND THE PHYSICIAN, THE DENTIST AND THE PHARMACIST.*

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The sixth edition of the National Formulary will soon become official and if the interest already shown in several of its new preparations is a criterion, the new book will prove a valuable asset to the physician, the dentist and the pharmacist. Certainly one senses to-day a greater feeling of coöperation on the part of these three professions, and it is not to be denied that the National Formulary may claim its due share in the development of this coöperation.

Development.—The N. F. was developed for the professions, a review of the several editions showing definite advances throughout its life. It is interesting to note that as far back as 1856 the AMERICAN PHARMACEUTICAL ASSOCIATION appointed a committee to collect "unofficial formulas in local use with many physicians of our union." However, there were so many formulas available for the same thing in substance, though differing in non-essential details of color, flavor, odor and proportions that the committee was unable to obtain favorable action on any specific one. Elixirs were just being popularized at that time, and the variations in this group resulted in the committee being dissolved. Years later, in 1883, there appeared two formularies, one on Elixirs, by John Uri Lloyd, and the other on local formulas of New York and Brooklyn, and these formed the basis for the first N. F. in 1888, known as the National Formulary of Unofficial Preparations. This title is interesting because it recognized a situation which still exists to-day. The United States Pharmacopœia was accepted as the official book and consequently the N. F. covered "unofficial" preparations. It acted as a stepping stone for the U. S. P., for if the latter provided standards and formulas of any article or preparation of the N. F., the authority of the latter ceased, as it does to-day. When the Food and Drugs Act made the N. F. and the U. S. P. official in character in 1906, the name of the former was officially changed to "The National Formulary."

Scope.—In the light of action taken by the N. F. VI committee, it is of interest to note that in the preface of the first edition of the N. F., a suggestion had been made to admit simple drugs or chemicals, but it was decided that the labor involved in the task already outlined was so great that no time could be devoted to any further additions. When it was suggested to the N. F. VI Committee that certain very popular simple drugs or chemicals be admitted, there were great misgivings on the part of many, it being claimed that the N. F. was established and had always been a book of formulas, and simples were out of place. Simples, however, had been admitted in the N. F. IV although only those which entered preparations and were not recognized by the U. S. P. were so included. On the other hand the N. F. was certainly trying to provide standards for the preparations which physicians were commonly prescribing and why should a popular item be omitted simply because it required no compounding or formula? Was not the public worthy of a

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standard of simples just as it was of a standard preparation? The final adoption of this proposed plan did not result in filling the new revision with everything in sight as many feared, but it did open the way for the proper recognition of such things as cerium oxalate, strontium bromide and many other very popular items.

Early in its deliberations the N. F. VI Committee agreed that "use by the medical profession" should decide what was to be admitted to the new book. This policy has been very closely observed and in order that there be a definite basis for the determination of this use, several surveys covering prescription ingredients were used. The largest of these reviewed about 121,000 prescriptions and from these several compilations the committee saw fit to delete 321 items which had been recognized in the N. F. V. Likewise 232 new monographs were added, most of which were products of extensive use, though some were required as pharmaceutical necessities in some form or another. Certain ones, like Syrup of Cherry, were added because it was felt that they would fill a valuable need in the armamentarium of the physician and the dentist. It should be understood that the National Formulary makes no claims of therapeutic efficiency for its many items, the fact that these items are extensively prescribed being considered all that is necessary to merit recognition. This policy is in direct contrast to that of the U. S. P. wherein every item, with the exception of pharmaceutical necessities and such preparations as vehicles, is definitely accepted upon its therapeutic value and proved merit.

The National Formulary is essentially a book of formulas, simples of both the U. S. P. and the N. F. being prepared in a manner convenient for administration. One who wishes to prescribe will thus likely find the item he desires available in a practical and palatable form, thus eliminating the necessity of being concerned, for instance, about the solubility of phenobarbital, whether it is water-soluble or alcohol-soluble and to what extent. In this particular instance one finds that a tasty elixir of phenobarbital is available representing $^1/_4$ of a grain of phenobarbital to each teaspoonful. The elixir is alcoholic since the chemical is not soluble in water. Or one may prescribe larger quantities of phenobarbital per teaspoonful by calling for the new iso-elixir which will be mentioned later. Thus solubilities are eliminated and incompatibilities are avoided. Thus also, one is not tempted to prescribe sodium phenobarbital in aqueous media, for, although it is soluble it soon decomposes and thus should preferably be used as a solid form of medication, as, for instance, in capsules or powders. Many other similar cases could be cited but time and space will not permit. Physicians and dentists are referred to the book or to their local pharmacists who will gladly coöperate in locating the most satisfactory form of administration for any specific item. Pharmacists must recognize that physicians and dentists are not as thoroughly acquainted with the official preparations as they are, and should therefore make every possible effort to pass on this information which is so mutually acceptable to all concerned.

NEW PRODUCTS.

While we may take for granted that every one is perfectly familiar with the general make-up of the N. F. and those products which have been handed down from the previous edition, there are many new preparations which are deserving of specific comment and these will be considered briefly.

VEHICLES.

For several years stress has been laid upon the numerous vehicles, elixirs and syrups of the N. F., and justly so, for they offer something as practical to the prescriber and the one for whom prescribed as is possible. That practical something is a tasty, palatable prescription, a simple thing which is so often sorely needed. Almost every physician is desirous of prescribing whatever medication is necessary in the most palatable and pleasing form, and a brief consideration of these N. F. preparations will open the way to better prescriptions. Every physician was not included in the previous statement, for it is known that there are certain patients who seem to require disagreeable and nauseating prescriptions, in order to be convinced that they are actually obtaining authentic treatment.

Syrup of Acacia.—Syrup of Acacia is a new addition and is presented as a specific vehicle and not just as a suspending medium in the old sense of the term. Acacia represents a colloidal type of product in which disagreeable substances may be dispensed, the colloidal action of the acacia preventing, in a large measure, the contact of the medication with the taste buds. Its use with substances such as urea should receive special consideration. It is flavored with vanilla and preserved with sodium benzoate. It might be added that a syrup prepared from whole acacia will produce a product superior in clarity and general appearance to one prepared from a powdered or granulated acacia.

Syrup of Cherry is another new addition to the vehicle fold, and one which has received very wide acclaim wherever it has been available. As a matter of fact it has received acclaim even where it has not been available and this situation has caused considerable annoyance. Its specific value lies in its fruity tartness, which makes it a delightful mask for some products such as the diluted acids, wherein the acid almost enhances the taste rather than destroys it. Unfortunately, the fact that the syrup is made from pure sour cherry juice and sugar will make it difficult at times to obtain the syrup in an off season. This very condition is found at the present time and it is regrettable, since it has been reported that many concoctions are being offered in lieu of the real syrup. Many of these, apparently, are likely not to simulate the true syrup in the least and thus will injure the legitimate use of the real material later on. The cherries which are used are the fresh, ripe, sour, pie cherries and not only the juice but also the crushed pits are included. The "open season" is not far away and from present indications it will be well for pharmacists to "stock up" and prepare for the busy twelve months ahead.

Syrup of Prepared Cacao or *"Chocolate Syrup"* is not a new syrup, although it has been markedly improved, but it is a valuable vehicle worthy of mention at all times. It is particularly desirable for the suspension and subsequent masking of insoluble substances, its heavy consistence materially aiding in preventing separation of the medication. It is often used with quinine salts. Its flavor and texture have been definitely improved.

Syrup of Cinnamon.—This also represents a vehicle which was previously official and, like syrup of chocolate, it has been improved from the pharmaceutical standpoint as it is now made by simple solution in place of the tedious percolation previously required. This syrup has come to be used specifically for the masking of the disagreeable taste of sodium salicylate. It offers a further advantage with the latter, since its natural dark color also masks the coloration so often observed with salicylate prescriptions in aqueous or colorless media.

Aromatic Syrup of Eriodictyon is again recognized and particular attention is called to its value as a vehicle for bitter drugs such as quinine and strychnine. Eriodictyon has been used for years as a mask for similar items and Dr. Bernard Fantus (1) has shown how it forms an insoluble and therefore tasteless product which is later readily assimilated. Dr. Fantus has been responsible largely for a number of these new vehicles and reference to the literature on a number of these products (2) would be well worth while.

Syrup of Glycyrrhiza.—This syrup is highly recommended for salty preparations such as the bromides. The natural sweetness of the syrup is followed by what has been termed a second sweetness due to the glycyrrhizin which is present. The preparation contains anethol, oil of fennel

and benzaldehyde in addition to fluidextract of glycyrrhiza. These added flavors enhance the natural flavor of the glycyrrhiza very materially.

Syrup of Raspberry, which has received such splendid recognition for its masking qualities of the salty preparations such as the bromides, is again recognized. Fifteen grains of a bromide per teaspoonful makes one feel that a pinch of salt has been added to bring out the flavor of the syrup. In this connection it might be well to state that syrups in general serve as the best masks for salty items, rather than plain water or elixirs which in fact intensify the saltiness.

This syrup, like syrup of cherry, is also prepared from the pure fruit juice and sugar. Consequently it, too, should be manufactured during the season of plenty. In the case of the syrup of raspberry, however, it is possible to obtain a concentrate which is made from the pure juice and sugar and this may be diluted with simple syrup and used, providing the finished product corresponds in color and taste to the one made by the original process and providing also that it produces a clear syrup on the addition of 50 per cent of alcohol.

Syrup of Thyme.—This syrup belongs to the vehicle class and offers a distinctive syrup for odor and taste, being more desirable for a change, even though the basic medication still may be the same.

A number of vehicle elixirs previously official have been recognized again. Among these there are offered vehicles of varying odors, tastes, alcoholic contents and colors. Thus one is able to change the vehicle from time to time while still maintaining the same medication throughout. This has been found to be a valuable feature in prescribing. Several such elixirs are as follows:

Compound Elixir of Almond, colorless, 4 per cent of alcohol; *Elixir of Bitter Orange*, yellow color, delightful taste, 28 per cent of alcohol which makes it valuable where high alcoholic content is necessary; *Red Aromatic Elixir* which is the aromatic elixir of the U. S. P. in a bright red jacket, alcohol content 23 per cent; *Compound Elixir of Cardamom*, pleasant flavor, colorless, 8 per cent of alcohol; *Glycerinated Elixir of Gentian*, yellowish brown, taste neither sweet nor bitter, alcohol content 13 per cent; *Compound Elixir of Vanillin*, amber color, very delightful odor and taste, alcohol content 8 per cent.

Aqueous Elixir.—Frequent objections have been raised over the presence of alcohol in many of the vehicle elixirs and there were many requests for a simple type of vehicle elixir without alcohol. These requests arose partly from the difficulty met in obtaining alcohol and partly from physicians who were desirous of having no alcohol whatever in their prescriptions. Aqueous elixir has been prepared to meet this demand. It is delightfully flavored, both odor and taste being very pleasant.

Iso-Alcoholic Elixir or Iso-Elixir provides a new innovation. It consists of a high and low alcoholic elixir both resembling aromatic elixir in odor and taste, and offering unlimited possibilities in prescription work. If an aqueous type vehicle is desired, the low alcoholic elixir, which contains about 10 per cent of alcohol, may be used, while the high alcoholic elixir with its alcoholic content of about 75 per cent may be employed for those substances which require a high percentage of alcohol for solution. The two elixirs are miscible and thus one may prepare a vehicle of any alcoholic strength between 10 and 75 per cent, dependent upon requirements. This feature has greater application than just to provide a solvent for a salt, however. Every one is familiar with the clouding produced when preparations like tincture of nux vomica or aromatic spirit of ammonia are prescribed with certain aqueous or even alcoholic vehicles. With Iso-Elixir available, it is prescribed as the vehicle, and the pharmacist, in filling the prescription, adjusts the amounts of the low and the high elixir so as to produce a product of approximately the same alcoholic strength as the tincture of nux vomica for instance, thus preventing any clouding effect. This is a decidedly forward step in the attempt to produce more elegant prescriptions. For convenience in calculating, a table is given which will aid in determining the quantities of each elixir to use.

AMPULS.

Twenty-eight of the most popular ampuls are recognized in the new N. F. together with quite an elaborate general chapter, covering the question of the selection of glass for ampuls, the preparation of the solutions, the technique of filling, sterilizing and testing for sterility. The individual monographs do not contain specific

formulas but contain tolerances, methods of sterilization and assay procedures. The tolerances are so worded that they apply to all sizes of ampuls. This section is a marked improvement for the book and places the manufacture of ampuls on the high plane where it rightfully belongs.

A special monograph has been included on *Redistilled Water*, which is required for ampul solutions. It produces a water which is practically free from pyrogens, that protein substance which is the cause of so much fever, discomfort and anxiety when used parenterally.

MEDICATED ELIXIRS.

In addition to the group of vehicle elixirs already mentioned, several new medicated elixirs have been placed in the N. F. VI.

Elixir of Aminopyrine contains about $2^1/_2$ grains of aminopyrine to each teaspoonful. It is pleasantly flavored with orange and contains approximately 20 per cent of alcohol. It has an attractive red color.

Elixir of Barbital, a dark brown elixir, flavored with the delightful compound spirit of vanillin, contains about 2 grains of barbital to each teaspoonful. The alcoholic content of the elixir is about 30 per cent.

Elixir of Phenobarbital is another of the new additions. It contains approximately $^1/_4$ grain of phenobarbital in each teaspoonful and it also is red in color. Its alcoholic content is about 20 per cent. It, too, is flavored with orange.

Elixir of Sodium Thiocyanate, or, as it is frequently designated, *Elixir of Sodium Sulfocyanate or Sodium Rhodanate*, has been added to the medicated elixir group. It contains $2^1/_2$ grains of the salt in each teaspoonful and is amber in color with a pleasant blended flavor.

EMULSIONS.

Several cod liver oil emulsions have been continued, of which the one with egg offers the finest type of preparation. An additional popular emulsion has been added, namely, *Emulsion of Liquid Petrolatum with Phenolphthalein*. This is a 50 per cent emulsion of heavy liquid petrolatum containing 1 grain of phenolphthalein to the average dose of a tablespoonful. It is emulsified with a combination of acacia and agar, so proportioned as to give a satisfactory product when prepared either by hand or by machine. The use of the hand homogenizer described in recent literature (3) produces an excellent product with a minimum of effort and is a sure guarantee to the pharmacist against "broken" emulsions.

GLANDULAR PRODUCTS.

Six glandular products have been recognized in the new N. F., namely, *Corpus Luteum, Ovary, Ovarian Residue, Anterior Pituitary, Whole Pituitary* and *Suprarenal*. The newly developed histological characteristics of the glandular products, so well prepared by Dr. Heber Youngken of Boston, opens an entirely new field in this line of work.

TABLETS.

Another one of the outstanding new features of the N. F. VI is the section devoted to tablets in which 48 new monographs appear. As in the case of ampuls, the monographs are primarily prepared as a means of control for the enforcement authorities and to provide uniform standards for manufacturers. No specific formulas are given, but the individual monograph is devoted to a tolerance statement

worded so as to cover tablets of all sizes, tests for identity and purity and a method of assay. For the most part, the tablets included are for simples only.

DENTAL PREPARATIONS.

A very valuable group of preparations of the new N. F. is that dealing with dental products. An associate committee of the American Dental Association consisting of Drs. Blayney, Aiguier, Dailey, Freeman and Timmons was primarily instrumental in the selection of these products for inclusion in the book and from preliminary reports we already know that its selections are most valuable.

N. F. Dentifrice or N. F. Tooth Powder comes first in the dental group. This is a basic powder only, composed mostly of precipitated calcium carbonate with only a trace of soap (5 per cent) and agreeably sweetened and flavored with a blend of soluble saccharin, oils of peppermint and cinnamon and methyl salicylate. This basic powder may be prescribed readily with sodium perborate or any desired medicament.

Glycerite of Iodine and Zinc Iodide, a modified or "Diluted Talbot's Solution" is next on the list. Every dentist is familiar with this popular preparation which has such marked antiseptic and astringent value in the treatment of pericementitis, gingivitis and lacerations.

Compound Dental Liniment of Aconite and Iodine is composed of 2 per cent of iodine, $2^1/_2$ per cent of fluidextract of aconite and 3 per cent of chloroform in a mixture of alcohol and water. It might be mentioned here that when a dentist prescribes tincture of aconite it is well for the pharmacist to consult him before dispensing the U. S. P. tincture which is 10 per cent, since the dentist invariably desires the once official tincture of 35 per cent strength. If this be the case, the prescription may readily be filled by using the proper amount of fluidextract of aconite carefully diluted.

Odontalgicum is the official Latin title for what was previously a toothache wax but is now a liquid under the English title of *Toothache Drops*. It is a solution of chlorobutanol in oil of clove and is extremely efficacious, each of the ingredients having marked obtunding properties. It should prove of marked value as a first aid for toothache.

Compound Paste of Acetylsalicylic Acid, popularly called "Dental Anodyne Paste," is a splendid dental anodyne for tooth sockets. It contains eugenol, which has a definite obtunding effect, peruvian balsam, which is antiseptic and promotes granulation, and acetylsalicylic acid which acts as an anodyne. These are incorporated in a base of white wax and wool fat. The directions for manufacture must be carefully observed lest the disagreeable separation of the balsam should occur, a problem which is familiar to most pharmacists and one which frequently causes difficulties.

Camphorated Phenol, composed of 30 per cent of phenol and 60 per cent of camphor in liquid petrolatum, is used as an antiseptic, devoid of topical irritation even to mucous membranes, in spite of its high phenolic content.

N. F. Aromatized Sodium Perborate is another one of the new dental items. It is agreeably flavored with oil of peppermint and soluble saccharin. Due to the large amount of this type of preparation being used by the layman without specific directions from a dentist or a physician, it might be well for the pharmacist to caution the customer about its promiscuous use when he sells the product. We realize how it has been the cause of severe mouth burns when used as a powder which lodges in cavities and eventually hydrolyzes to sodium hydroxide.

Solution of Procaine Hydrochloride, a sterile 2 per cent solution of the salt in normal saline solution, is a popular dental anesthetic. Solution of epinephrine hydrochloride is usually added in small amounts just before use. The latter gives a bloodless working field and prolongs the action of the procaine.

One or two additional products are of particular interest to the dental profession. *Alkaline Aromatic Solution* is a standard mouth wash of an alkaline character. *N. F. Antiseptic Solution*, which as you note has a slightly changed title, has been fortified as far as its antiseptic properties are concerned by the addition of chlorthymol. A few minor changes have also been made in the formula.

MISCELLANEOUS.

In addition to the many new items previously mentioned there are others of marked interest together with changes in old preparations, changes in titles and other general points of revision which can only be noted by a careful study of the book. Certain of the additional new monographs might be mentioned, however, and further details may be obtained later. Among these are *Solution of Boric Acid*, which is one of saturation; *Solution of Nux Vomica Alkaloids*, which is an aqueous solution prepared for veterinary use; *White Lotion*, which is the popular formula of the dermatologists and not the veterinary product as heretofore; *Syrup of Potassium Guaiacolsulfonate*, which contains about 5 grains of the salt per teaspoonful in aromatic syrup of eriodictyon; *Compound Ointment of Benzoic Acid*, or *Whitfield's Ointment*, which was greatly in need of uniform standardization; *Ointment of Coal Tar*, which contains 5 per cent of coal tar in paste of zinc oxide; and finally *Ointment of Scarlet Red*, which contains 5 per cent of scarlet red.

From the foregoing it must be admitted that the new National Formulary has been markedly revised and has something of vital interest for every one concerned. The physician will find a solution to the ever-present question of how to improve the palatability of his prescription and he will also find many popular items made available with a standard, uniform formula, the same in Maine as in Southern California. The dentist also will take advantage of these same items and in addition, the numerous specialty preparations made available primarily for dental use. The pharmacist will be in a position to suggest these items and to supply them to the several professions, thereby not only assisting the several professions, but the general public as well, to say nothing of the automatic development of his own professional standing.

REFERENCES.

(1) JOUR. A. PH. A., 4, 323 (1933).
(2) *Ibid.*, 7, 698 (1934); 8, 812 (1934); 8, 915 (1934); 1, 46 (1935).
(3) *A. J. P.*, April 1935.

LATIN-AMERICAN DELEGATES HOLD CONFERENCE AND SYMPOSIUM ON THE PHARMACOPŒIA.

The national Directors of Health of the Pan-American Conference and other representatives of the Health Departments of the Latin-American countries were in conference at the Pan-American Sanitary Bureau in Washington during the week of April 5th.

As the Spanish translation of the new United States Pharmacopœia has been undertaken as an official act by the Pan-American Sanitary Bureau and is now well under way with considerable material in the form of proof, the Latin-American delegates were invited to participate in a conference and symposium on Pharmacopœias.

The invitation was extended by the officials of the AMERICAN PHARMACEUTICAL ASSOCIATION and the delegates were the guests of the ASSOCIATION for the conference, followed by a reception.

President Walter A. Bastedo, of the Pharmacopœial Convention, presided at the conference and welcomed the delegates, and outlined the objectives of the Board of Trustees in preparing a Spanish edition of the United States Pharmacopœia.

A number of the delegates responded expressing their appreciation of the service which the U. S. P. Board had rendered in supplying the latest scientific standards for a large number of im-