COMMITTEE REPORTS

REPORT OF AMERICAN PHARMACEUTICAL ASSOCIATION COMMITTEE ON U. S. PHARMACOPŒIA (1928).*

BY LYMAN F. KEBLER, CHAIRMAN.

There seems to be a dearth of suggestions available among the members of this committee. It may in part be due to the fact that a goodly number are members of the Committee of Revision and for that reason do not consider it prudent to discuss the various problems that might come to mind, outside of the committee activities.

As the result of a circular letter sent to the various members of the committee, the chairman has reeeived a number of suggestions, however, believed of sufficient importance to incorporate into a report. William Mittelbach feels that there is something inherently wrong somewhere because of the fact that the Pharmacopœia, the most complete textbook on the subject in the world, is but seldom referred to in a majority of the drug stores. Mr. Mittelbach is a veteran and has been exceedingly active during his long connection with the drug business. He considers it very unfortunate that conditions at present obtaining crowd out the Pharmacopœia. He feels that the younger generation is not given sufficient opportunity to make original investigations but is compelled to devote its apprenticeship to matters far remote from real pharmacy.

PHARMACOPŒIA SHOULD INCLUDE MORE DRUGS.

Dr. H. H. Rusby has written rather extensively on plant drugs in the Pharmacopœia. He believes in the inclusion in the Pharmacopœia of a much larger number of drugs in common use, if for no other purpose than to provide adequate standards of purity. In this connection he writes:

> "Nevertheless, I still hold that the pharmacists' rights in the Pharmacopœia are infringed by denying them U. S. P. standards for drugs in common use, and I claim that quite a number of drugs (which are named in my publication) should be reinstated in the Pharmacopœia."

In his writings he expressed the view that the founders of the Pharmacopœia did not intend that the usefulness of a drug should be taken into consideration in deciding upon its admission. In this connection he now believes himself in crror and writes:

> "* * * I must modify my statement that the founders of the Pharmacopœia did not intend that usefulness of a drug should be taken into consideration in deciding on its admission. It is evident they did intend this factor to be considered."

The Doctor has a distinct aversion to the word "proved" as constituting a basis for admission. On this point he writes:

> "I also object strenuously to the word "proved" as constituting the ground for admission, as it can be used to exclude drugs which have not been investigated which would be found acceptable if they were investigated. I think the word "probable" should be substituted, probability, added to extensive use being a sufficient ground for acceptance."

LITIGATION AND THE ERGOT PROBLEM.

During the past year the subject of ergot has claimed considerable attention at the hands of the Doctor. He feels that the Department of Agriculture, by not stringently administering the food and drugs act was admitting ergot into this country which is prejudicial to the health of our citizens. He has taken the Department rather sharply to task on several occasions. A litigation was started by an importer and is still pending in the District of Columbia against the Secretary of Agriculture, endeavoring to enjoin the Secretary from admitting certain kinds of ergot into this country held to be in violation of the food and drugs act. In connection therewith, Dr. Rusby filed an affidavit in behalf of what he considers a standard kind of ergot as against ergot that he considers inferior; ergot which does not comply with the Pharmacopœial standard, provided for in the body of the text under Ergot.

* Presented at Portland, Me., A. PH. A. meeting, 1928.

Another point raised from time to time is contained on page 4, General Notices, under the heading of "Vegetable Drugs" and reads in part; "They are to be free from mouldiness, show no discoloration, abnormal odor, sliminess or deterioration due to any cause." The contention is, that that requirement excludes all mouldiness, discoloration and deterioration in every container, bale, package or what not in every shipment. The question naturally arises, is such a strict interpretation to be placed on this clause, or shall the enforcing officers be allowed to use some judgment and discretion. Permit me to say, that if the first construction is to obtain, the difficulties of importing or shipping crude drugs into interstate commerce will be considerably increased. It seldom happens that a shipment of such drugs is entirely free from the abnormalities referred to above. Is it practical? Let us hear from the trade and the committee of revision. In connection with a standard in Pharmacopœia VIII, a large importer wrote regarding a detention made on the findings of a leading authority:

> "To go into the foreign markets to secure an article of Digitalis of which we import many tons each year, with an effort to get only goods which are collected from plants of the second year's growth at the commencement of flowering, may be aptly compared to securing the left hind leg of a rabbit, killed by the light of the moon, in a grave-yard by a cross-eyed negro."

The biological test has stepped in and settled this issue.
On the subject of Ergot, Dr. Rusby has the following additional information to offer:

> "On the subject of ergot, I now have something definite to submit. It is now conclusively proved that an ergot that has not suffered damage, resulting in the reduction of its activity, is at least twice as active as required by the present cockscomb test of the Pharmacopœia. It has been clearly shown that the standard fluidextract on which that test is based was made from ergot a part of which has suffered much damage. I urge most strongly that this standard be changed so that only 0.3 cc. of the fluidextract shall be required to darken the cockscomb."
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> "I also assert the strong probability that two samples which agree in their strength as determined by the cockscomb test, may differ widely in their oxytocic activity, and I advise the most thorough investigation to determine whether there should be separate tests to establish these two kinds of activity."

Your chairman is not prepared to believe that the standard fluidextract on which the test is based was made from ergot a part of which had suffered much damage. Such a condition would certainly reflect seriously on some one. The question of ergot apparently requires more study.

Dr. E. N. Gathercoal believes that the report of the committee should cover the activities of the sub-committee on Botany and Pharmacognosy, and possibly the investigations under the direction of Chairman Cook. Your chairman does not believe that this comes within the province of our committee but constitutes a part and parcel of the report of Chairman E. Fullerton Cook.

CHANGING OINTMENT NAMES AND FORMULAS.

W. Bruce Philip writes:

> "Our members believe it inadvisable to change the base of ointments—as, from yellow vaseline to white, or *vice versa*, whereby confusion is bound to arise and the possible benefit from the change seems questionable, especially where Pharmacopœias have seemed to alternate with each edition on changing the basis of certain preparations."

The subject of ointments in the U. S. P. X, has received considerable adverse criticism. It seems that only two of the ointments appearing in the U. S. P. IX have found their way into U. S. P. X without change of either composition or title. Such numerous changes must present many difficulties. It would hardly seem probable that changes in composition have been made solely on the basis of certain fatty substances being more readily absorbed than others. If this was a deciding factor it must be said that this whole field is still very much in the realm of opinion and undue changes in formula should not be made on such a basis. A number of years ago sheep

wool fat was supposed to be supreme, now we are not so certain. These changes present problems not only for the physician who uses ointments in his practice, the druggist and the consuming public, but also difficulties in connection with the enforcement of the Federal and State food and drug laws.

NOMENCLATURE AN IMPORTANT MATTER.

The question of nomenclature is an important matter. The changing of names or titles is always liable to introduce confusion. This is particularly true in the case of drugs. For example, hexamethylene tetramine became known to the medical and pharmaceutical world under the proprietary title of urotropine. The British Pharmacopœia in 1914 recognized it under the title hexamine, the U. S. P. IX, called it hexamethylenamine and the U. S. P. X revision names it methenamine. This all makes for confusion. Fortunately, the drug is not a virulent poison. Otherwise serious results might follow through misunderstandings in the writing and compounding of prescriptions. The point your chairman desires to emphasize is that there should be as few synonyms as possible of a given drug in any given language. The same drug should be known the world over under the same name in the English speaking and writing world. Changes in name should be resorted to only as an extreme necessity.

While discussing nomenclature your chairman desires to call attention to the phrase "Olive Oil Castile Soap," in U. S. P. X, used as a synonym for a soap made from olive oil and sodium hydroxide. It is the old, old method of making castile soap. This synonym injects a new element of confusion. By inference it means that there are other kinds of castile soaps. For example, cotton-seed oil castile soap, palm-olive castile soap, palm-cocoa castile soap, etc. Some manufacturers claim that a better soap can be made with oils and fats other than olive oil. If this is correct why, in the name of good business, handicap a superior soap with a name that is hoary with age and represents something inferior? The Federal Trade Commission has had the castile soap controversy under consideration for several years. Thousands of dollars have been spent by both the Government and the trade. One manufacturer compiled a most extensive bibliography on the subject. The vast majority of the references define castile soap as a soap made only with olive oil. An attempt was made by manufacturers at a hearing to have the question of castile soap settled on the basis of the information contained in the U. S. Pharmacopœia X. It presented a unique problem. It allowed for scores of different castile soaps. An early decision is awaited with interest.

STANDARDS AND MISBRANDING.

A member of this organization testified to the effect that if only 5% of olive oil were used in the manufacture of a soap, such a soap could properly be called castile soap. This position does violence to long established principles obtaining in the enforcement of Federal and State food and drug laws. Examples: Food Inspection Decision 75, 1907, "The terms 'maple sugar' and 'maple sirup' may only be used on the label as part of the name when those substances are present in substantial quantities as ingredients. They should not appear on the label as part of the name when only a small quantity of those substances is used to give a maple flavor to the product." Food Inspection Decision 63, 1907, "It is held that if a mixture of drugs is named after one or more but not all of the active medicinal constituents (not vehicle) present in a preparation, the word 'compound' can be used in connection with the name, (*a*) provided the active constituent after which the product is named is present in an amount at least equal to that of any other active medicinal agent present. Or (*b*) provided the potent active constituent after which the product is named is present in sufficient amount to impart the preponderating medicinal effect. Example: If a product is named after the active constituent, strychnine, the strychnine or one of its salts should be present in sufficient amount to produce the preponderating medicinal effect of the preparation." The present official Pharmacopœia recognizes at least two products that transgress these decisions, *viz.*, "Compound Pills of Mild Mercurious Chloride," and "Compound Licorice Powder." The National Formulary V contains several more. As an example, attention is called to "Compound Syrup of Figs." The active agents in this syrup are senna and cascara. The fig extract simply adds agreeableness. Reference is made to the National Formulary here because both publications are legal standards, are intimately interwoven and for the reason that a member of our committee introduces it later.

Preparations having names in conflict with the above decisions are considered misbranded

under the National Food and Drugs Act. If the legal standards themselves contain products that are misbranded under these decisions, what effect will they have in the enforcement of the act? Your chairman believes that this paradoxical condition should be rectified as soon as practical. The standards should lead the way. They should not handicap the work.

MODIFY U. S. P. AND N. F. PREPARATIONS CLASSED AS ALCOHOLIC BEVERAGES.

Mr. Philip believes that Pharmacopœial and National Formulary preparations now classed as beverages by the Government, should be sufficiently medicated with as little change in the proportion of the ingredients as possible so as to eliminate the necessity of accounting for same by annoying bookkeeping and endless details. Among the preparations included in the list may be mentioned:

U. S. P. **Elixir Aromaticum** (Elixir Aromatic).
N. F. **Elixir Anisi** (Elixir of Anise).
N. F. **Elixir Aromaticum Rubrum** (Red Aromatic Elixir).
N. F. **Elixir Aurantii Amari** (Elixir of Bitter Orange).
N. F. **Elixir Cardamomi Compositum** (Compound Elixir of Cardamon).
U. S. P. **Elixir Glycyrrhizæ** (Elixir of Licorice).
N. F. **Elixir Taraxaci Compositum** (Compound Elixir Taraxacum).
N. F. **Elixir Terpini Hydratis** (Elixir of Terpin Hydrate).
N. F. **Spiritus Aetheris Compositus** (Compound Spirit of Ether or Hoffmann's Anodyne).
N. F. **Spiritus Myrciæ Compositus** (Compound Spirits of Myrcia).
N. F. **Tincture Amara** (Bitter Tincture).
N. F. **Tincture Aromatica** (Aromatic Tincture).
U. S. P. **Tinctura Aurantii Dulcis** (Tincture Sweet Orange Peel).
U. S. P. **Tinctura Zingiberis** (Tincture of Ginger).

Your chairman is thoroughly in sympathy with this idea but does not believe it practical in some cases. Everything possible should be done to lessen the burden of both the druggists and prohibition enforcing officers.

SUBSTANDARD DRUGS MAKE FOR TROUBLE.

In connection with the use of a so-called non-alcoholic simple elixir Mr. Philip writes:

> "Members are violating the Pure Food and Drug Law by using, without referring to the physician, a non-alcoholic simple elixir. The pharmaceutical houses are in part to blame; for they have, through their representatives, sold this product and by telling the druggist that everybody is doing it, have unintentionally caused this condition. A doctor in prescribing simple elixir does not know what he will receive—from one store an alcoholic preparation, in the next store a non-alcoholic preparation."

This brings up the knotty and often aggravating problems of the so-called substandard U. S. Pharmacopœia and National Formulary drugs, provided for under the Federal and various State laws. These laws, in short, provide standards, then promptly knock them down. Your chairman has always believed that this proviso works to the disadvantage of physicians and the sick and is liable to get the trade into trouble. It has made trouble for some. He has used his best efforts to have it eliminated without success. The justification of this proviso has often been made that it enables a manufacturer to put a superior product on the market without violating the law. There may be a few such cases but on the whole it makes for substandard drugs and ultimate trouble for some one.

In order to meet conditions obtaining the Bureau of Chemistry in 1916 issued the following Service and Regulatory Announcement:

> "180. *Labeling of U. S. P. or N. F. Articles Not Conforming to Standard.* With reference to the labeling of drugs recognized in the United States Pharmacopœia or National Formulary but which do not conform to the standard of strength, quality or purity, as determined by the tests laid down therein, in the opinion of the bureau, the label should bear either a statement to the effect that the drug is not a United States Pharmacopœia or National Formulary article, together with a state-

ment showing its own actual strength, quality or purity, or a clear and exact statement of the nature and extent of the deviation from the standard of strength, quality or purity set out for the article in the United States Pharmacopœia or National Formulary."

Mr. Philip seems to feel that the Pharmacopœia is too often modified by the mere whim or caprice of some person who desires to inject his personal opinion into the book in order to make it look a bit different. He thinks that our aim should be a correction of errors rather than a correction of the formulas.

U. S. P. BOOK OF STANDARDS THAT MAKE FOR GREATER THERAPEUTIC USEFULNESS.

The U. S. Pharmacopœia is primarily a book of standards but standards that make for greater therapeutic usefulness and efficiency. If it were not so why spend all of the time, energy, money and effort in its get up. The inclusion of certain drugs of little or no recognized medicinal value, at the present time, often causes material embarrassment in the enforcement of certain Federal laws. The deletion of certain drugs in the last revision brought material relief. It is believed that several more could be omitted with advantage.

In some of the work with which your chairman is connected, it is quite common to meet with ingredients in various products for which most unreasonable medicinal claims are made. When it is pointed out that certain drugs have little real medicinal value, reference is made to the fact that they are now or have been included in the U. S. Pharmacopœias or National Formularies, recognized standards under the Food and Drugs Act. This, of course, at times presents added barriers to overcome. One must admit that if a drug is accepted for inclusion in either of these publications, it should have sufficient merit medicinally to justify its recognition. If it is desired to include a drug of doubtful or no recognized medicinal value, at the present time, just for the purpose of providing a standard of purity, it would seem desirable to add a statement to the effect that it possesses little if any recognized or known medicinal value at the present time. Several publications have adopted this practice and it is proving very useful.

CHARLES NICOLLE AWARDED NOBEL PRIZE.

The recipient of the Nobel Prize in medicine and physiology for 1928, is Charles Nicolle, French bacteriologist. He is best known as discoverer, in 1912, that typhus is conveyed by inoculation, by lice, fleas, etc., from a patient to healthy persons. Dr. Nicolle was awarded the Osiris prize of 100,000 francs for the same discovery, which is said to have saved a million lives during the World War.

The recipient has been for twenty-five years chief of the Pasteur Institute in Tunis, and during the greater number of these years he carried on the work, which led to the discovery, and because of this the decision of the medical faculty of Karolina Institute came as somewhat of a surprise, as the prizes have heretofore been awarded for contemporary discoveries; the momentous value of the discovery is not questioned and the award is rightly bestowed.

BENZOYL-MORPHINE RESTRICTED.

The United States is among 12 nations which have adopted the plan of the League of Nations for the control of benzoyl-morphine, according to an announcement by the League of Nations which has been received at the Department of State.

The Geneva and Hague Opium Conventions provided for the control of products which in the light of subsequent scientific investigations may prove to be susceptible to abuse, as are morphine and cocaine.

In December 1927, the League Council in the recommendation of the Health Committee (which had previously consulted the Public International Health Office), asked the Governments to bring eucodal and dicodide within the provisions of the Geneva Opium Convention, since, in the opinion of the Health Committee, they were habit-forming drugs liable to be abused in ways similar to the abuse of morphine or cocaine.

In June 1928, the Council of the League, on the recommendation of the Opium Commission, further decided to make a similar recommendation to all the States, signatories of the Geneva Convention, as well as to all States, parties to the Hague Opium Convention, concerning benzoyl-morphine which is another derivative of morphine.

INTERNATIONAL PHARMACEUTICAL FEDERATION.

Brief mention is made of some of the transactions of the International Pharmaceutical Federation in the August JOURNAL, page 815.

It was decided not to include preparations of potent drugs in the International Formulary as these properly belong in the contemplated International Pharmacopœia.

Further information is to be set relative to the standard moisture content of powdered digitalis for which the content had been fixed at a maximum of 3%.

The standardization of less potent drugs is a subject of further study. Professor Wasicky gave as an example Ceylon cinnamon of which quite a number of varieties are known in commerce varying in price and properties. The standardization of such drugs might be determined by organoleptical examination, gum content and that of bitter content. A commission consisting of Professors Wasicky, de Graff and Herrisey was appointed to study the subject and to devise methods of examination which could be carried out by pharmacists. The latter submitted notes on the action of certain heterosides (glucosides) which by their decomposition cause blackening of dry plant tissues. Special reference was made to ambroside and asperuloside.

Messrs. Collard and Linstead made a number of suggestions for a standard pharmacy law. In pharmacy laws the public health should be the first consideration. On the continent of Europe university training is compulsory and this training is better organized than that at the schools of pharmacy. Professors at the University enjoy a higher status than that held by teachers in schools and they would object to changes in other positions. From the students' point of view it is desirable that they should follow the same courses as other students in science so as to receive a good grounding in general science. It was accepted by the meeting that there should be a central control of the practice of pharmacy and that inspectors should be pharmacists and that it would be advisable to have special tribunals to deal with legal questions consisting of lawyers and pharmacists and such tribunals should have disciplinary power. The point was quite generally held by the members that no special assistant's examination was necessary but that a certificate of competency for the duties of an assistant to a pharmacist in a laboratory should be issued. It was accepted as an axiom that only qualified chemists should own pharmacies, and further, association for business purposes with unqualified persons should be prohibited. Permission should be given to medical practitioners to dispense medicines only when there was no pharmacist in the neighborhood. Only pharmacists should be allowed to dispense medical prescriptions and sell drugs, though an exception could be made in the case of poisons and other substances required for agricultural or domestic use. The manufacture of pharmaceutical specialties should only be carried on under the control of a responsible pharmacist.

The report submitted by Messrs. Swicker, Heuberger, Stich, Martin and Madsen recommended the universal acceptance of names of proprietary chemicals included in the United States, British and Dutch pharmacopœias, such as barbital, glusidum, etc. The Commission pointed out that short names are more convenient for use by physicians in every-day practice than are long scientific names. A further discussion of the subject is to be made at the next meeting of the Federation. The same action was taken on the international control of pharmaceutical specialties, following the report submitted by Dr. Risin. So many preparations are being put out by manufacturing houses that it is necessary to have close coöperation of pharmacists and manufacturers. Pharmacists are responsible for what they sell and therefore the composition of these preparations should be indicated on the label. It was further decided that the subject be taken up internationally by having the several countries nominate members to a commission for the discussion of the question and to make suggestions for a uniform method of control.

The Dutch Pharmacopœial Society proposed the appointment of a Commission to investigate the various conditions affecting the supply of medicines, etc., for shipments. The Federation acted favorably on the proposition and appointed Messrs. Van Itallie, H. N. Linstead and M. Vavasseur, as members of the Commission.

The influence of trade on the practice of pharmacy was discussed and this question also was carried over to the next meeting for further consideration.

Stockholm was selected for the next place of meeting, in 1930.