THE THEORY AND ART OF PHARMACOPŒIA REVISION, IN THE INTEREST OF PHARMACAL SERVICE.*

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THE THEORY.

The theory of this important subject is based on the following fundamental principles:

1. The general object and function of the Pharmacopœia are the same as they were originally, in spite of changes in method and detail, resulting from changed conditions.

2. The object is the safety and welfare of the sick and of the interests of physicians and pharmacists, in order that that object may be better attained.

3. The Pharmacopœia is not a therapeutical work and its only legitimate attention to therapeutics is to see that the articles in use are genuine, pure and of standard quality.

4. Each successive edition should be an improvement upon its predecessor, in the factors of scope, nomenclature, methods and scientific and linguistic accuracy.

5. Scientific and linguistic accuracy should not be limited to important practical matters. The revision of the Pharmacopœia is supposed to be performed by the highest representatives of medicine and pharmacy, and the credit of these professions forbids that accuracy of detail should be ignored when it does not involve some practical objective. The definitions of the Pharmacopœia should be complete in themselves, including by their language the whole of the article defined and excluding all else.

6. Changes from a preceding edition that are not based on the above considerations are objectionable, and should not be made lightly, or without full consideration.

7. Pharmacopœia revisers should be thoroughly familiar with the researches and their results of preceding Committees, to avoid useless repetitions and the possible reversal of former correct conclusions.

8. The Pharmacopœia is essentially a book of standards for medicinal agents in common use, these standards being maintained by it through the use of the physical, chemical and biological tests that it provides for this purpose, and of prescribed processes of manufacture and preparation.

9. In providing these requirements, full attention must be given to the legal responsibilities involved, especially to the fully established principle that the courts cannot sanction a departure from the Pharmacopœial requirements on the ground that the requirements are erroneous. The courts have often ruled that the language of the Pharmacopœia must be followed, even though that language is such that it defeats the object for which it was framed.

10. The Pharmacopœia is complete in itself, not being associated with any other similar work, unless such work is the product of its own procedures, carried out with full authority over both works, and producing both with full consideration that they are parts of one whole. In other words, there is no authority

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whatever for the repudiation by the Pharmacopœia of any part of its responsibility, notwithstanding that the statute may impose a similar responsibility on some other agency.

THE ART.

The art of Pharmacopœia revision is based on an exhaustive study of the above principles, in all their bearings, and in the device of such methods as will most efficiently employ these principles in the work of revision. It forbids the employment in Pharmacopœial revision of anyone who is not fundamentally and effectively conversant with this subject. Yet we have seen men engaged in Pharmacopœia revision who were disqualified in nearly all of these directions, and it is doubtful if a majority of the workers on any revision have been fully conversant with the results of the investigations conducted by previous committees. The last mentioned defect is probably responsible for more Pharmacopœial errors than all others combined.

Let us consider the United States Pharmacopœia, as it stands to-day, and see what evidence it presents of having been revised in accordance with the principles that have been enunciated. Since it is my intention to confine myself, on this occasion, to the defects in the work, I will say at once that this revision is a great improvement on its predecessor and is, on the whole, an admirable work. I believe, however, that the revision is fundamentally wrong in certain directions, and that it contains many serious defects that should be corrected.

Under principle number one, we note that all historical data available prove the original object of the Pharmacopœia to have been that stated in principle No. 8, but we have seen the gradual substitution of two totally different and wholly unjustifiable objects, (*a*) the recommending to the medical profession of those medicines which a certain number of the medical men on the Committee of Revision think should be used, and (*b*) the creation of a false belief, especially in foreign countries that those not admitted are not used here. The latter objective may be condemned on simple ethical grounds. The former is a gross violation of the third principle, as it is the conversion of the Pharmacopœia into a work of therapeutic claim and controversy. Not only have we had conclusive evidence that some of these claims, as to both value and the absence of it, have been crroneous, with a probability of many other such cases, but we know that the airing of such opinions is no part of the office of the Pharmacopœia. The only ground that can properly justify the inclusion of an article in the Pharmacopœia is the protection of the patient who uses it, as to its standard character, and the only one that can justify its exclusion is the fact of its insufficient use. No State or federal statute has the slightest ground or excuse for saying that its provisions for the saftey of citizens shall be limited to that of the patients of certain physicians or of a certain class of physicians. Undoubtedly, the therapeutics of the eclectic physician are, on the whole, inferior to those of the regular school, although, under the present growing neglect of the study of materia medica by the latter, this condition is likely to become reversed. The important fact is, however, that the patients of eclectics have the same claim to statutory protection as any others. We might as properly restrict the laws against robbery and assault to the patients of a certain class of physicians as the protection of the Food and Drugs Act.

But it is not only the patient who is placed in peril by such limitations in the treatment of medicinal agents. The statute holds the pharmacist strictly responsible in his relations with the patient. This responsibility exists quite as clearly, though not so explicitly expressed, in the case of a non-official as an official article. The very object of official treatment is to give the pharmacist the means of meeting this responsibility. To refuse this assistance is to place him, as well as the patient, in jeopardy. Hence the latter part of my title, which refers to pharmacal service, this including the interests of both.

Our fourth principle provides for proper delections as articles go out of use or for inclusion as new ones come in under the influence of modern knowledge. This principle cannot be considered aside from Nos. 5 and 6.

The subject of nomenclature has been very greatly neglected. The fact that the general principle of botanical nomenclature—or rather the absence of any principle—is fundamentally wrong and in conflict with that applied to zoölogical names, may be overlooked, as it is in accord with an international agreement to employ certain designated incorrect names. I should rather see our own Pharmacopœia independent enough to be accurate in this, as in other things, but there are two sides to this question, and I am willing to conform to custom, on the expressed understanding that we know we are wrong and yield to convenience. What I should like, however, is a frank admission of the fact in the preface of the book, so that more careful authors, who refuse to employ inaccurate names, even by agreement, should not be placed in a false position by Pharmacopœial authority.

Quite aside from this mooted question, there are glaring cases of violation of accepted rules of nomenclature. Consider the adoption of the purely Spanish title "Cascara Sagrada" as the Latin title and the relegation of "Rhamnus Purshiana," which is purely Latin, to serve as the official English title! The purely Latin title Balsamum Tolutanum is assigned to the English position, while "Tolu," an utterly barbarous name, occupies the Latin position. We might refer here to far worse things done by the National Formulary. "Guaiacum," formerly the title of Guaiac Wood, while the resin had to be called "Guaiac Resin," or "Guaiaci Resina," has now become the designation of the latter. In a similar way, the titles of Iris versicolor and Orris have been transposed, notwithstanding that one is innocent and the other decidedly poisonous.

This brings us to remark that, for many successive revisions, one of the first procedures of the leaders was to secure the adoption of a rule, that, while changes in the definitions should be made in the interest of scientific accuracy, the safety and convenience of the public required that changes in titles should not be made except for urgent reasons. The abandonment of this principle is one of the indications of the decline of the safe conservatism that formerly ruled.

Coming to the subject of scientific and linguistic accuracy, we find the present edition of the Pharmacopœia contains many such inaccuracies.

The definition of Glycyrrhiza well illustrates this class of errors. The name "Glycyrrhiza glabra" means one that is destitute of trichomes, while "Glandulifera" means one that is covered with glandular trichomes. Thus, when we say "Glycyrrhiza glabra, variety glandulifera," we mean a plant without any trichomes that is covered with trichomes! It is quite possible that one knowing these plants only externally might regard one as a variety of the other, but not if he

has examined them histologically. However, even in that view, the definition might be shortened gracefully by saying "varieties of Glycyrrhiza glabra, having a yellow and sweet wood." The expression now used is "yielding" a yellow and sweet wood, the word "yielding" not being well chosen.

The present definition and description of Myristica violates almost all of the principles here enunciated. During the reign of a former revision, a lot of nutmegs were seized, at the Port of New York, by the Bureau of Chemistry, because a tuft of mold was found in the cavity at the end. It was established that no nutmegs are ever imported that are free from this condition, but this knowledge could not change the fact that the shipment was in violation of the legal standard. The Bureau, of course, has the option of refraining from making further seizures, but to just that extent it must ignore the Pharmacopœia and place the latter in an apologetic position. Those familiar with these facts secured a mention, in the succeeding revision, of this peculiarity of nutmegs, thus giving them a legal standing, but at the most recent revision this was deleted, showing that the member responsible for the present definition was not well-informed on the history of the subject.

The situation is even worse with the definition of tar, as "a product obtained by the destructive distillation" etc. If a definition does not define, it performs no office. This definition does not tell us which of the scores of "products" of this process is the one intended. The only defense that can be rendered is that the description gives this information. If this reply were to be formulated, it would say "There is no use of having a definition if the description is sufficient." If this is true, then the definition should be omitted altogether, for it is far less discreditable to the revisers to have no definition at all, than to print one that is without meaning or effect. How have the mighty fallen when such careless methods are substituted for the fine scholarly work of such a man as Charles Rice!

Our third proposition, that the Pharmacopœia is not a therapeutical work, has never been denied or questioned in terms, although many times it has been reiterated in pharmacopœial publications. Nevertheless, to reject an article in common medicinal use by physicians, because a majority of the physicians in the revision committee regard it as not therapeutically useful is quite as definitely making the book a therapeutical authority as it would be in describing the uses of the article. But our revisers have gone farther—very much farther—than this, for they reject articles unless their therapeutical usefulness has been "proved." That is to say, an article prescribed by the vast majority of American physicians, but the therapeutical usefulness of which is not accepted as "proved," may be deleted from the Pharmacopœia, as was done with Chenopodium and its oil. Furthermore, no statement is made, nor is there even any implication, as to when or by what method such therapeutic usefulness must be proved, nor who is to be the judge of the sufficiency of such proof. If any reader can suggest a possible case of greater indefiniteness or general looseness of language than this, let us have it. Let it be noted, also, that this language does not refer to an insignificant matter of verbal expression, but to a practice that is to leave millions of patients on whom such articles are used, whether recognized by the U. S. P. or not, to be deprived of the safety and benefit for which the Pharmacopœia exists, and to leave thousands of pharmacists exposed to the danger of prosecution. All

that is necessary in order to secure the deletion of an article from the Pharmacopœia under this provision is for some member of the Revision Committee to deny its usefulness and then to refuse all proof to the contrary. And what is the object of all this? Merely to justify a few men who believe—rightly in most cases, it must be admitted—that their judgment in such matters is superior to general practice. The Pharmacopœia is not the place in which to carry out their missionary work. Physicians' textbooks and other publications constitute the medium for imparting therapeutical instruction. If physicians are too indolent or incompetent to reform the practices of their professional brethren, the sick people of the United States are not the ones to be penalized, even potentially, for this failure.

The habitual and gross violation of principle No. 6, is doubtless chiefly due to a disregard of No. 7. To the experienced student of Pharmacopœial changes, it is perfectly obvious that persons with no knowledge of the reasons that have led their predecessors to adopt certain statements and expressions, have casually made changes of language here and there for the mere purpose of "doing something," and without either knowledge or judgment concerning the consequences of their own work. Again and again we have seen the painstaking care of eminent scholars who have labored with past revisions, carelessly destroyed by those who had not reviewed the studies and investigations on which the results had been based.

Little need be added to the enumeration of our ninth principle, unless it were to recite the numerous decisions of courts which support it. It is a pity that some of us who are frequent witnesses in court cannot find time to compile a digest that would indicate clearly what must be expected when the plea is made that a U. S. P. provision is erroneous and should be disregarded. More than once, I have heard a judge repudiate the suggestion that he had authority to alter or minimize the statutes. I have even heard one say to an attorney, "You might prove to me that the requirement of the Pharmacopœia is so worded as to defeat its own purpose; to result in actual danger, while your departure from it is beneficial, and still I have to decide that you have violated the law." I have personal knowledge that some of our U. S. P. revisers have no adequate conception of the importance of this consideration. They appear to take the ground that an error in the text is of no practical moment, because it can be overlooked in practice. Even if this were true, and it must be admitted that often the law is ignored, still it would be shameful for our Pharmacopœia to be placed in a position where the most charitable thing that can be said of it is that it is irresponsible. It is still worse when this position is deliberately taken in advance by the revisers, yet it is undeniable that this has been done when just corrections have been offered and have been rejected.

The most important part of this paper is its discussion of principle No. 10, since this is the point concerning which the largest number of people responsible for Pharmacopœial policy and procedure are the most widely astray. I fail to understand why it is so difficult to secure acceptance of the fact that there is no logical or practical ground whatsoever for a division of work of the same kind between the U. S. P. and the N. F. Aside from all practical considerations, it is a blot upon the intelligence of both American medicine and American pharmacy

that such an idea should exist among representative members of these professions. The establishment of the National Formulary, to do the work that it was intended to do, was an important accomplishment, but its present procedure is very injudicious when sincere, and very vicious when not.

Let us consider some of the things that might happen to occur. The first of them is not a mere possibility, because we have several concrete examples of it. Physostigma was dropped from the U. S. P., doubtless with the expectation that it would be taken up by the N. F., but this was not done. We now have the extract of this drug, a favorite medicament of many excellent physicians, in the N. F., with no official recognition, description or standard for the drug from which it is made! And why should this not be the case? What right has the U. S. P. to assume what the N. F. people are going to do? There is no official connection between them, and there should be none, unless a single body should revise both works. There are other and similar instances to that of Physostigma, and there might be many more. As a matter of fact, the Revision Committee of the U. S. P. has no guarantee whatever of the continued publication of the N. F., or that, continuing to be published, it will continue to include the drugs deleted from the U. S. P. The fact is that the whole of that kind of work that is performed by the U. S. P. should be done by it and that only work of a different kind should be performed by the N. F. If the N. F. Committee desired and cared to do its full duty to the people of the United States, it would refuse to take up any crude drug or similar article when deleted by the U. S. P. and it would join in a concerted effort to compel that book to perform its legal duty. In case the U. S. P. Committee repudiated this public obligation, suppose that the pharmacists of the nation were to respond by repudiating the U. S. P., by declaring that the N. F. should be made complete in itself, and should publish a complete Pharmacopœia that would include all commonly used drugs, whether they are already in the U. S. P. or not! There is no organic reason why this should not be done. It is true that people are too sensible to adopt such a course, but the U. S. P. is not on this account any less responsible for it as a potential act than as an actual one. Then, indeed, we should have a double standard, but the situation, as to principle involved, would not differ at all from what it is at present.

There is but one rational and, on the whole, but one practical method of correcting the evil position in which American pharmacists have placed themselves by their too ready submission to the dictates of a small group of medical men, and that is to make a complete separation in the character of the work of the U. S. P. from that of the N. F., and then to see to it that each performs its full duty to the public. It is true that we can resort to makeshifts, and become a body of time-servers, adopting one wrong procedure after another to counteract the evil effects of the preceding one.

Let it never be forgotten that a hundred pharmacists make actual use of the U. S. P., for important purposes, for every once that a physician so much as looks at it; that probably a majority of the physicians of the United States do not know the difference between the Pharmacopœia and the Dispensatories, and that 95 per cent of them never saw a copy of the Pharmacopœia. Whose interests are at stake under such conditions? Not those of either of these two professions, but of the patients served by them. These patients are affected a thousand times

more frequently through the use made of the Pharmacopœia by pharmacists than through such use by physicians. How can any intelligent and sincere person be in doubt as to whose services should be facilitated by this great national legal authority?

It is my desire to study carefully through the text of the Pharmacopœia for the detection of violations of all these principles, but of what avail will this be unless the Committee is fully committed to the policy of observing them?

Convinced as I am that it is the duty of all pharmacists and of all well-intentioned physicians to restore the U. S. P. to the full measure of its former usefulness, I offer the following resolutions for adoption by the New York Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION, and I call upon our brother pharmacists in all sections of the country to secure similar action by their schools and associations of pharmacy.

1. *Resolved*, that the term "pharmaceutical necessity," as used in the U. S. P. shall be construed as meaning that the book shall include all articles that the professional pharmacist is commonly expected to supply; that in place of the term "proved therapeutic usefulness" there be substituted that of "common therapeutic use," that the U. S. P. should contain standards for all crude drugs and similar legitimate medicinal articles believed by the Committee on Revision to be sold in twenty-five per cent or more of the pharmacies or drug stores of the United States, in their crude condition, or in the form of preparations, or of both.

2. *Resolved*, that we use our best efforts to secure the appointment of delegates to the next Pharmacopœia convention who shall go instructed to secure the adoption of this resolution or one of similar purport, as a basic rule of procedure for the next Committee of Revision.[1]

PHARMACISTS OF FIFTY YEARS AGO HAD THEIR PROBLEMS TO SOLVE THE SAME AS PHARMACISTS OF TO-DAY.

The *Chemist and Druggist*, of February 5th, reprints an article under "Superfluous Pharmacy," which appeared in this publication Feb. 15, 1877. It reads: "Days of perplexity and trial are at hand for the retail pharmacist. The stores have snipped off a percentage from his sundries and patent medicines; a benevolent association strives to close his doors at an early evening hour; and now a fair city is about to rise where there shall be the least possible ill-health. 'I have projected a city,' said Dr. Richardson, 'which shall show the lowest mortality. Our city, which may be named Hygeia, has the advantage of being a new foundation, but it is so built that existing cities might be largely modelled upon it.' The promised land has emerged from the shadows of a Social Science lecture, and here it is spread out before us on the table mapped and planned, with broad streets and gardens, a mile of sea front, good drainage and comfortable dwellings. The estate is called Courtlands, and is situated close by Worthing. Should the plan succeed, the druggist must seek out some other occupation and take himself and his galenicals to a less favored spot. Serious misgiving must be felt at this novel application of the motto, 'Habenda ratio valetudinis.' "

PRODUCTION OF ATTAR OF ROSE IN BULGARIA.

According to estimates, the production of attar of rose attained about 1600 kilos in 1926, an output slightly smaller than that attained in 1925. Of the total about 1000 kilos were produced in factories, and the other 600 kilos in peasant homesteads. It is claimed that almost all of this production has been sold or contracted for sale.

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[1] These resolutions were unanimously adopted.