

CHANGED ALKALOIDAL STANDARDS IN U. S.
PHARMACOPŒIA IX.

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For reasons which seemed to the members of the Revision Committee good and sufficient, the alkaloidal standards for a number of official preparations have been changed in the newly issued U. S. Pharmacopœia IX. The pharmacist consequently has on his shelves tinctures, fluidextracts and extracts which met the requirements of U. S. Pharmacopœia VIII, but which are no longer of official strength.

It is to be noted that the old standards, except in the single instance of preparations of opium, were inelastic. Extract of *Nux Vomica* should be found to contain 5 percent of strychnine; Tincture of *Cinchona* should contain in each 100 Ćc. 0.75 Gm. of the ether-soluble alkaloids of *Cinchona*, etc., no maximum or minimum limits being prescribed. In the new Pharmacopœia, on the other hand, while in nearly all cases a definite standard is fixed for each product, a certain margin of variation from this standard is permitted. Thus, Extract of *Nux Vomica* is to be made to contain 16 percent of the combined alkaloids of the drug, but an extract may be dispensed which contains as much as 16.8 percent or as little as 15.2 percent of these alkaloids. Some will maintain that the minimum figure in each case will become the standard for the product. Unquestionably there will be a tendency towards this result, yet manufacturers of pharmaceutical products will keep in mind the facts, first, that variations in the results of alkaloidal assays, made even by experienced chemists, make it unsafe to adopt a minimum standard, as long as there are scores of drug inspectors keen to discover sub-standard products, and, second, that more or less deterioration occurs in galenic preparations, so that the leeway allowed by the Pharmacopœia is none too great in practice.

Hence in comparing the new standards with the old, it would be a mistake to take for the former the minimum figures of the text.

We shall be disappointed if we expect to gather any information about the intention of the Committee in fixing the new standard from a comparison of the average doses given in the text. As a rule we shall find that where there has been a change of even as much as 25 percent in the standard for a product, its average dose remains unchanged. But now and again we find changes in the dose where no change has been made in the standard.

In some cases it is impossible to fix an exact ratio between the old and new standards, owing to change in the basis of the standard. Thus for *Cinchona* preparations the basis is now simply the total alkaloids of the bark, whereas it was formerly the ether-soluble alkaloids, the proportion of which to the total alkaloids being exceedingly variable. *Nux Vomica* has heretofore been standardized on the basis of its content of strychnine. In the new Pharmacopœia the basis is the combined alkaloids of the drug, on the assumption that these consist of brucine and strychnine in equal proportions. An exact ratio between these bases cannot be predicated; the best we can do is to fix arbitrarily a ratio of 5 to 2 as a rough approximation to the truth.

Opium presents a difficulty in the fact that the new Pharmacopœia, conforming to the general practice in Continental Europe, adopts as its basis Anhydrous Morphine, whereas hitherto we have been accustomed to use morphine

containing one molecule (over six percent) of water of crystallization. Heretofore powdered opium (the "opium" recognized in the Harrison Narcotic Law) has been required to contain not less than 12 nor more than 12.5 percent of crystallized morphine. These figures would correspond respectively with 11.28 and 11.75 percent of anhydrous morphine, average 11.52 percent. The new standard is not less than 10 nor more than 10.5 percent anhydrous morphine, average 10.25; but this latter figure has not been made explicitly and authoritatively *the* standard.

The Pharmacopœia provides only that opium of higher percent than 10.5 may be brought within the required limits by admixture with powdered opium of a lower percentage or with some inert diluent. This seems to give authority for making the actual standard as low as 10 percent, and inasmuch as this is the standard generally recognized in Europe, it seems highly probable that this will become by common consent the accepted standard in America. However, it will be as well here to assume the average figure of 10.25 percent—corresponding with nearly 10.77 percent of crystallized morphine—about seven-eighths the old standard.

During the next few months, there will be frequent occasion to reduce to the present official standard of strength preparations that were standardized in accordance with the U. S. Pharmacopœia VIII or to calculate the quantity of the old preparation equivalent to a prescribed amount of the new. In all such computations the average figures only should be used.

It is convenient to have at hand a table of ratios for the several preparations in question, by aid of which problems of this kind can be readily solved, and such a table is here offered.

ILLUSTRATIONS OF USES OF THE TABLE.

I. To adjust the strength of a fluid preparation of U. S. Pharmacopœia VIII to the new standard:

(A) If the new standard is lower than the old, simply add of the menstruum used in making the preparation, the percent indicated in Column II of the table example. To adjust to the new strength (*i.e.*, 1 Gm. anhydrous morphine in 100 mils) one pint of tincture of opium, add 15.6 percent of diluted alcohol = $(16 \times 0.156 = 2.496 \text{ fluidounces} =)$ 2 fluidounces + 238 minims, making 18 fluidounces, 238 minims.

(B) If the new standard is higher than the old, the volume of the fluid must be reduced by the percentage amount indicated in Column II of the table. The method of procedure is as follows: Take out from the tincture or fluid-extract double the percentage quantity shown in the table, evaporate this to a thin syrup and add enough alcohol to bring the volume to one-half what it was originally and add this to the remainder of the original fluid. The proportion of alcohol in the product will not vary greatly from that in the original fluid. It is not advisable, however, to make the adjustment in this manner in the cases of fluidextracts of Ipecac and Jaborandi, where the difference in standard exceeds 20 percent.

Example.—To adjust to the new standard one fluidounce of tincture of belladonna root take out 22.2 percent (twice the 11.1 percent given in the table) = 107 minims; evaporate this to a thin syrup and add alcohol to make up a measure of 53.5 minims ($=107 \div 2$) and add this to the remainder of the original fluid, making a total volume of $426\frac{1}{2}$ minims.

II. The strength of a solid preparation can be adjusted to the new standard only when that standard is lower than the old, the adjustment being made by adding the requisite percent from Column II of the table of glucose or milk sugar as the case may be.

III. To find the quantity of a product made in accordance with U. S. P. VIII that is the equivalent of a given quantity of the corresponding official product U. S. P. IX, use the data of Column II of the table.

Example.—Required the equivalent old formula, of 275 minims of Fluid-extract Ipecac, U. S. P. IX. According to the table add $33\frac{1}{3}$ percent ($275 \times 0.333 = 91.7$ minims); $275 + 91.7 = 366.7$ —practically 367 minims. Required the equivalent old standard of 4 fluidounces (1920 minims) of official Tincture of Opium. By the table, subtract 13.5 percent ($1920 \times 0.135 = 259$ minims.); 4 fluidounces - 259 minims = 3 fluidounces 221 minims.

TABLE OF RELATIONS OF OLD TO NEW U. S. P. ALKALOIDAL STANDARDS:

Preparation	Column I Old to new (product).	Column II New to old (equivalent).
Extract Belladonna Leaves	+ 12 percent	- 11.6 percent
Extract Hyoscyamus	+ 20 percent	- 16.7 percent
Extract Nux Vomica	- 22 percent	+ 28 percent
Extract Opium	- 6 percent	+ 6.3 percent
Powdered Opium	+ 13.8 percent	- 12.1 percent
Fluidextract Aconite	- 20 percent	+ 25 percent
Fluidextract Belladonna Root	- 11.1 percent	+ 12.5 percent
Fluidextract Cinchona	Indeterminate	Indeterminate
Fluidextract Guarana	- 12.5 percent	+ 14 percent
Fluidextract Hyoscyamus	- 11.5 percent	+ 13.3 percent
Fluidextract Ipecac	- 25 percent	+ 33.3 percent
Fluidextract Pilocarpus	- 33.3 percent	+ 50 percent
Tincture Aconite	- 10 percent	+ 11.1 percent
Tincture Belladonna Leaves	+ 16.7 percent	- 14 percent
Tincture Cinchona	Indeterminate	Indeterminate
Tincture Hyoscyamus	+ 8 percent	- 7 percent
Tincture Opium	+ 15.6 percent	- 13.5 percent
Tincture Opium Deodorized	+ 15.6 percent	- 13.5 percent
Tincture Physostigma	+ 6.7 percent	- 6.3 percent

When a regiment is under march, the rear is often thrown into confusion because the front does not move steadily and without interruption. It is the same thing with business. If that which is first in hand be not instantly, steadily and regularly dispatched, other things accumulate behind, till affairs begin to press all at once, and no human brain can stand the confusion.—*Walter Scott.*