Pharmacopeial Assays of Drugs and Galenicals.

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Discussions on the standardization of drugs have, of late years, claimed much attention in medical and pharmaceutical literature. The object of the present paper is not to review the entire field covered by the arguments, but merely to present a few considerations which have not heretofore been dwelled upon, or which, in the writer's opinion, have not received the consideration they deserve, yet in view of the nearness of the pharmacopeial revision, should be thoroughly examined and carefully weighed.

The unbiased observer must acknowledge that the pharmacists, as a class, have honestly endeavored in the past to perfect the processes of the Pharmacopeia and to render the galenical preparations as uniform in composition and as permanent as possible; the revisions of the National Pharmacopeia during the past fifty years bear ample testimony to this fact. Even processes of assay were introduced at the request of pharmacists. They made their appearance for the first time in a modest way in the Pharmacopeia of 1860, which required that "*Opium* (crude) should yield at least seven per cent. of morphia by the officinal (Staple's) process;" and the quality of *scammony* was defined by requiring that "ether dissolves at least 75 per cent. of it; and when the ether has been evaporated, the residue, dissolved in a hot solution of caustic potassa, is not precipitated by dilute sulphuric acid."

Both these processes are in consonance with the character of the Pharmacopeia as a law book, and in following them, the product obtained by the one could only consist of morphine contaminated with some narcotine; and the results of the other could only be due to scammony resin provided that well-characterized opium and scammony had been subjected to the assays. In other words, the processes were in the main correct, but the Pharmacopeia had omitted to describe the material which should be subjected to these tests.

The Pharmacopeia of 1880 supplied this deficiency, and it has also improved the morphiometric test for opium. According to our present knowledge, opium, as described by the Pharmacopeia—when examined by the process laid down by the same authority yields as a final product the alkaloid morphine in a reasonable state of purity; no other alkaloid—at least none of those ordinarily occurring in drugs—can be present; the process is adapted for morphine, but for no other alkaloid.

The old process for the assay of scammony has been retained, and coupled with the pharmacopeial description of the drug, excludes other ether-soluble convolvulaceous resins, even orizabin (jalapin of authors) which has been shown to be chemically identical with scammonin. For the resin of the orizaba root can not be manipulated so as to have the physical characteristics of the scammony obtained by the spontaneous evaporation of the latex of the living scammony root.

In the two cases cited the requirements are clear and unmistakable, as a legal requirement should be, and it will be observed that such is also the case with the few other drugs for which processes of assay have been introduced into the last Pharmacopeia.

The officinal process for determining the digestive strength of *pepsin* may not be the best that can be devised; but in connection with the described physical characteristics, identifies the article with sufficient exactness, and establishes a minimum standard of quality which is perfectly reliable for the conditions given.

On assaying *cinchona* bark for total alkaloids by the pharmacopeial process, the resulting product consists of quinine, cinchonine and allied alkaloids, provided the identity of the bark, as being derived from a species of cinchona or of remijia, has been established; for by the same process a number of poisonous alkaloids may be prepared; and if, for instance, a strychnos bark (some of which are now met with in commerce) were tested in the same manner, styrchnine and brucine would finally be weighed. It follows from this that if cinchona bark or its powder had become accidentally mixed with strychnos bark, the alkaloids of the latter would be weighed as cinchona alkaloids. The same is also true of berberine, hydrastine, and some other non-poisonous alkaloids which are not freely soluble in a solution of sodium hydrate.

The pharmacopeial estimation of *quinine*, which is based upon the sparing solubility of its sulphate in water, excludes all other alkaloids likely to be met with, even berberine sulphate being more freely soluble in neutral aqueous liquids; but if crystallizing, would reveal its presence by its yellow color. It will thus be seen that, while the pharmacopeial requirements for the percentage of quinine are, according to our present knowledge, sufficiently perfect as a legal standard, the assay for total alkaloids can be thus regarded only in connection with the absolute identity of the drug itself.

The remaining drug for which the present Pharmacopeia prescribes a process of assay is *jalapa*, which is required to contain at least twelve per cent. of resin, of which not over ten per cent. (1.2 per cent. of the drug) should be soluble in ether. These requirements should be considered in connection with those given under *resina jalapæ*, excepting the faulty one with ammonia water, and are sufficient to establish the identity and purity of the drug and the product obtained. Incidentally it may be remarked that the German Pharmacopeia, which requires a minimum of only ten per cent. of resin, will probably reduce the amount to eight per cent., and the same may be necessary in this country, although it is well known that roots of much higher grade *may* be found. As it is likely that the subterraneous part of the plant will survive the winters in most sections of the Southern and Central United States, it is to be hoped that its cultivation, which appears to present no difficulties or unusual labor, may be undertaken, so that a supply of better quality of the drug may be regularly obtainable. In regard to the ether-soluble portion of the drug, it is well known that its percentage varies; but in the past experience of the writer it rarely exceeds ten per cent. of the total resin, and is mostly less than this amount. Since the water-soluble portion of the *alcoholic extract* of jalap possesses decidedly purgative properties, it may, however, be questioned whether an assay of the drug, based solely upon its resinous constituents, can secure the absolute uniformity of other galenical preparations than the officinal resin, and it is obvious that for preparing the latter a previous assay is not necessary.

In suggesting the standardization of other pharmacopeial drugs, writers have usually selected such which contain alkaloids, and for determining the percentage of the latter, recommended, in most cases, either the volumetric estimation of the liberated alkaloids by acids, or the employment of Mayer's solution. Though this test liquid is an excellent reagent for alkaloids, it cannot lay claim for giving unvarying results, since these are in many cases affected to a considerable extent by different degrees of dilution. And since its general behavior to all alkaloids is alike, the precipitates obtained with it from acidulated solutions merely prove the (probable) presence of alkaloid without identifying it. Such a process evidently lacks the first requisite of a legal requirement, definiteness; for pharmacopeial purposes it would be applicable only to the drug as there described, but not to the powder, tincture, extract or other galenical preparations.

But is there really such an urgent necessity, overpowering every other consideration, for requiring all drugs furnished by nature to contain a definite percentage or a minimum amount of a certain constituent, or mixture of constituents? This is extremely doubtful for all those drugs which can be readily identified by their physical characters, and which have not been subjected to fraudulent manipulations. The three species of cinchona formerly recognized by most pharmacopeias, viz.: *C. Calisaya*, *C. succirubra* and *C. officinalis*, furnish unobjectionable bark for pharmaceutical purposes, and no assay—indispensable though it may be to the manufacturer of quinine—would be necessary for the uses of the physician or pharmacist; the introduction of barks, many of them of very poor quality, obtained from botanically allied trees, and possessing similar microscopic characters, rendered the identification of the former doubtful, and chemistry was called upon to supply the needful means for determining the main constituents without regard to origin.

Why the quality of commercial jalap has deteriorated, is not known; possibly Prof. Fluckiger's suggestion (see March number, p. 142) may be correct, and since