the fraudulent manipulation (if the drug has been subjected to such) has been skilfully concealed, the necessity exists for the estimation of the remaining resin.

The milk juice of scammony root became adulterated in former years through the cupidity of the importer limiting the purchasing price to a figure below the cost of production, no less than through the cupidity of the producer.

Even at the present time we have no definite knowledge of the extent to which the composition of the pure milk juice of the poppy varies in the different districts of Asia Minor; but it is known that the opium from various localities may vary in morphine strength to the extent of several hundred per cent. Moreover, its original characters as an exudation are entirely obliterated by the manipulations it is subjected to before it enters the market; its physical characters approach those of the extracts, the external appearance of which indicating their remedial qualities only to a limited degree.

Now, let us briefly consider one of the most powerful drugs in the Pharmacopeia, *nux vomica*. This seed is easily recognized, and its freedom from admixtures may be established without difficulty. It has been frequently the subject of chemical examination, and two of its powerful alkaloids, strychnine and brucine, are well known and are met with in commerce; yet the residuary products left in the manufacture of these commercial alkaloids, have never been satisfactorily examined, although they have been shown to contain notable quantities of both strychnine and brucine; they still await researches similar to those made by Liebig and others, and later by O. Hesse, into the nature of the residuary products of quinine manufacture. But granting, for the sake of argument, that the two alkaloids named fairly represent the total alkaloidal constituents, it has been found that the total percentage of alkaloids varies in the commercial article generally between 2.5 and 3.5. In a sample of Bombay seeds, Dunstan and Short determined (*Year book*, 1883, p. 235) 3.90 per cent., and in one specimen (*ibid.*, 1884, p. 163), taken directly from the fruit, 5.34 per cent. was obtained. Now, regarding the ordinarily best results with commercial samples (3.5 per cent.) as pure strchnine, one-twelfth grain of this alkaloid would be represented by 2.38 grains of nux vomica; or, by double this amount (4¾ gr.) if styrchnine be regarded as constituting one-half of the total alkaloids. All these quantities are within the limits of allowable large doses; but no prudent physician would *commence* with such doses of such a potent medicine.

There is still no process known by which strychnine may be absolutely and completely separated from the other strychnos alkaloids. Dragendorff (*Werthbestimmung*) regards the two principal alkaloids as being present in approximately equal proportion. Dunstan and Short (*loc. cit.* 1883, p. 469) have followed a method of separation which, in their hands, has given approximately correct results. On calculating the relative percentage of strychnine to the total alkaloids, as determined by them from commercial tinctures and extracts, it will be found to vary for the tinctures between 32.7 and 49.8 per cent. and for the extracts between 35.8 and 50.1 per cent., the extremes being in the proportion of 2 to somewhat over 3. It is known that brucine has an action, which is, qualitatively, very similar to that of strychnine, but quantitatively, differs very materially, according to Falck *being weaker in the proportion of 38.5 to* 1. Calculating, upon this basis, the activity of brucine, into strychnine, the latter would be represented, instead of the mixed alkaloids, by the figures 31.5 and 51.4, the proportion of the lowest and highest, or weakest and strongest being very nearly the same as before, 2 : 3. It is evident, therefore, that the determination of the total alkaloids will *not* secure the asserted uniformity, it will even not lessen the uncertainty to any appreciable degree. The uncertainty would be considerably reduced, though not entirely removed, if an absolutely reliable assay of strychnine could be made, and until this is accomplished, physicians will have to continue to prescribe the alkaloid strychnine or one of its salts, if they aim at producing definite effects, which they believe not to be obtainable from nux vomica or its preparations, owing to the inherent variation in their *composition*, whether the drug be standardized for total alkaloids or not. There would be no harm done if the Pharmacopeia would require, say not less than 2.5 per cent. of total alkaloids, but the necessity for it is not apparent since it will be difficult to find in commerce nux vomica containing a decidedly smaller amount. It should also be stated in this connection that, in the writer's experience, the amount of strychnine obtained in the manufacture on a tolerably large scale, is usually considerably less than might be expected from the figures given above.

It seems unnecessary to enter in a similiar manner into details with regard to other drugs containing alkaloids. When examined into without bias, it will be found that the different alkaloids present in the same drug, if qualitativey of the same action, usually differ considerably in their quantitative effects; that not unfrequently the qualitative effects of such alkaloids (for instance in aconite, veratrum, etc.,) differ from one another very markedly; and that for both these reasons a knowledge of the total amount of alkaloids can not give a correct idea – on the contrary, must be frequently misleading—as to the value of such an assayed product compared with the effects of its principal medicinal alkaloid in an isolated condition.

A practical difficulty for such assays on the scale required for the pharmacist consists in the correct sampling of the drug. Different specimens of aconite root, of nux vomica, of the narcotic leaves, etc., taken from the same parcel, will be found to give results differing more or less, and to preserve in several samples taken from the same lot, the relative proportions of old and young roots, or of rhizomes and rootlets, will prove to be a most arduous task. In one assay giving an account of their excellent researches on nux vomica (*loc. cit.* 1884, p. 163), Dunstan and Short state that "the alkaloidal content of the seeds is directly as their size, and inversely as their number in the fruit." These are conditions which pharmacopeial requirements can not influence, one way or *another. It is obvious, then, that a* correct and uniform sampling of such drugs can only be accomplished by grinding the parcel and mixing intimately in other words, by destroying the physical identity of the drug.

Other difficulties might be mentioned, but, in the writer's opinion, those cited appear to be the most prominent ones. Some excellent suggestions on this subject were presented to the British Pharmaceutical Conference in 1884, in two papers written by Mr. H. F. Schacht and by Mr. D. B. Dodd (*Year book*, 1884, pp. 180, 185), they discuss in a clear and unimpassioned, but convincing manner, the claims for standardization and some of the fallacies, and are in marked contrast to some papers which made their appearance more recently on this side of the Atlantic.

In the beginning of these remarks I stated that in the past, pharmacy had endeavored. I now add that she honestly continues in her endeavors to perfect pharmacopeial processes, and to render galenicals as permanent and uniform as possible. To reach the theoretical perfection, a great deal of labor will have to be performed, and many intricate researches will have to be carried out to a successful issue, by physiologists, by therapeutists, by chemists and by pharmacists. In the meantime, ordinary prudence demands that a praiseworthy object should not be jeopardized by laying a treacherous foundation, and that the Pharmacopeia should not sanction processes which in their results, *do not and can not prove that at* which they aim, and consequently introduce uncertainties, and even sources of danger, equally great or greater than existed before.

In closing these remarks, I can not more fittingly summarize them, than by quoting the conclusions arrived at, from a different starting point by, Mr. Schacht in the paper cited above. "Bodies of definite chemical composition and their dilusions are eligible for standardizing, but preparations of the nature of vegetable infusions (drugs) tinctures, extracts, being for the most part mixtures of indefinite and unknown agencies, cannot be standardized without risk of misleading. Whenever any one of this latter class of bodies has been so studied that the remedial potencies and chemical properties of all its elements are declared by authority to be well known, that one passes from the latter class *into the former*." *Am. Jour. Phar.*