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ACID-INSOLUBLE ASH STANDARDS FOR CRUDE DRUGS.*

BY CLARE OLIN EWING AND ARNO VIEHOEVER.

Having had occasion to review analyses of a considerable number of domestic and imported crude drugs with regard to their content of ash and acid-insoluble ash, the attention of the writers was called to a number of instances where a striking discrepancy occurred between the general run of analyses and the U. S. Pharmacopoeia and National Formulary Standards. In some instances it appeared that the present standards were somewhat rigid, whereas in others the ash standard was placed so high as to excite suspicion that a sample of the product in question yielding such an ash would be extremely dirty. It appeared, furthermore, that determinations of the ash insoluble in 10 percent hydrochloric acid would often disclose the true condition of the material, as regards cleanliness, and that an ex-

* The changes of existing standards and the establishment or adoption of new limits as standards, suggested in this manuscript, should be considered as an expression of our personal opinion and not as an official announcement of the Bureau of Chemistry.

tension of ash standards, including limits for acid-insoluble ash, would be very much preferable to the present standards.

The requirement of a standard for ash in connection with vegetable crude drugs is comparatively modern. It seems to have been first introduced practically simultaneously in the U.S. Pharmacopoeia VI (1882) and the German Pharmacopoeia II (1882). There was apparently considerable commercial opposition to the inclusion of such ash standards and the expansion of the practice proceeded rather slowly; in the U. S. Pharmacopoeia VIII (1905) there were a trifle less than thirty. The last Pharmacopoeial Revision Committee appears to have been fully converted to the practice, and there are only a few exceptions in the present revision (IX) where standards for ash are given; among these, however, are such important drugs as cascara sagrada, hydrastis, wild cherry, sanguinaria, and black haw. The Committee went even a step farther in its efforts to insure clean drugs and in a few instances included standards for acid-insoluble ash, notably in the cases of Saigon and Ceylon cinnamon (ash 6 percent, acid-insoluble ash 2 percent), black pepper (ash 7 percent, acid-insoluble ash 2 percent), and senna (ash 12 percent, acid-insoluble ash 3 percent), although oddly enough, no method for its determination is given. We are convinced that this is a rather serious omission, and that not only should a method be inserted in the Pharmacopoeia, but the practice of including insoluble ash standards should be extended, in support of which opinion a number of specific examples are cited herewith:

Asafoetida.—The U. S. Pharmacopoeia allows the use of either starch or magnesium carbonate as diluents in order to maintain the powdered form of asafoetida; in order to allow for the presence of magnesium carbonate the ash limit of the powdered asafoetida is raised from the 15 percent of the whole drug to 30 percent, although, if starch were used, an extremely dirty product, when powdered, would comply with the 30 percent standard. It is of interest in this connection, that although crude asafoetida may yield as low as 5 percent or less of ash, samples have been noted which yielded over 50 percent. Attempts have been made to import some lots yielding over 15 percent but less than 30 percent, for use in the preparation of the powdered drug. We believe this to be contrary to the intent of the Pharmacopoeia. In order to obviate these possibilities, the use of magnesium carbonate might well be discontinued, and starch only be specified. By so doing the same ash standard could be enforced for the powdered as for the crude drug. The occurrence of material containing such high amounts of ash indicates lack of care in collection, and is strong presumptive evidence that the collector may have been none too scrupulous regarding the source of his material; in fact, in a number of instances asafoetida which was found to be extremely dirty, also failed to comply with all of the U. S. Pharmacopoeia tests of purity, notably the ferric chloride test for foreign resins. The adoption of a standard for acid-insoluble ash would serve to discourage the importation of extremely dirty material. Such a standard would not even interfere with the use of magnesium carbonate as a diluent, inasmuch as this substance is soluble in the acid solution and only the dirt, sand, pebbles, etc., would be revealed by that determination.

Hydrastis.—Thirty-one commercial samples of hydrastis root showed a range of 4.49 percent to 17.81 percent of total ash, and 1.27 percent to 11.22 percent

acid-insoluble ash[1]. It was noteworthy in this connection that the samples of genuine whole root generally yielded lower percentages than the powdered specimens. The nature of the product is such that one would of course expect that certain amounts of earthy material might be included in the commercial handling of the drug, but obviously such a high amount as the 11.22 percent above noted is beyond all reason. At the current price of over $5.00 per pound a person buying a 100 pound lot of the drug would be paying over $50.00 for valueless material. It is of interest in this connection that the Austrian (VIII, 1906) and Swiss (IV, 1907), Italian (III, 1909) and Netherland (IV, 1905) pharmacopoeias all have an ash standard of 6 percent. While only few samples which we had under observation came up to this foreign standard of 6 percent, it should be remembered that golden seal root is one of the few domestic drugs which is exported to these European countries in large amounts, and there appears no reason why the drug used in the home trade should not be collected and handled with the same care as that which is designed for export. We feel also that in a case like this where the drug is so expensive, it is of especial importance to provide not only a suitable standard for total ash, but also one for acid-insoluble ash. We would therefore suggest that a standard of 8 percent (or possibly even 6 percent) for total ash, and also a limit of 2.5 percent for acid-insoluble ash be adopted.

Hyoscyamus.—Hyoscyamus is also a comparatively expensive drug and should have an ash standard lower than the present limit of 30 percent. The German Pharmacopoeia (V, 1910) has a limit of 24 percent, the Austrian (VIII, 1906) of 20 percent; this latter figure may be somewhat rigid—Wilbert[2] has stated that the Austrian Pharmcopoeia has been severely criticized for its generally low ash content requirement for drugs and that the figures cited there are largely academic.

Newcomb's data[3] are of especial interest since he examined both commercial samples of Hyoscyamus and carefully cleaned material, which he had grown himself in the medicinal garden of the University of Minnesota. From his data the variation in ash content of different parts of the plant is evident, but the results are also suggestive with regard to the effect of cleaning.

ASH CONTENT OF HYOSCYAMUS.

	Part of Plant.	Source.	Percent of ash.
(1)	Basal leaves, 89% Flowering tops, 11%	Commercial sample	21.69
(2)	Basal leaves, 89% Flowering tops, 11%	Commercial sample	19.97
(3)	Flowering tops	Select commercial sample	9.88
(4)	Flowering tops	Select commercial sample	9.48
(5)	Flowering tops	Select commercial sample	9.54
(6)	Flowering tops	Select commercial sample	9.06
(7)	Basal leaves, first year	Medicinal plant garden	16.02
(8)	Basal leaves, first year	Medicinal plant garden	16.17

[1] Analysts: Mr. Elgar O. Eaton, San Francisco Station; Mr. Hugo I. Wichmann, Denver Station; Mr. F. O. Woodruff, Boston Station; Mr. C. K. Glycart, Chicago Station. (All of the Bureau of Chemistry.)

[2] Wilbert, M. I., J. A. PH. A., 1, 457, 1912.

[3] Newcomb, E. L., Belladonna and Hyoscyamus," *Amer. Journ. of Pharmacy*, 87, 8, 1915.

Analyses of 12 commercial samples made by different analysts of the Bureau of Chemistry showed a range of 18.2 percent to 30.52 percent of total ash, and 11.6 percent to 19.05 percent of acid-insoluble ash.

Based upon the data at hand, an ash standard of 24 per cent, supplemented by an acid-insoluble ash standard of 12 percent would appear to be suitable and should conduce toward greater cleanliness in this product. In conversation with a number of growers and large commercial users of hyoscyamus the writers have been informed that it would be entirely practicable in a commercial way to comply with such limits.

Mustard.—Within the past several years the writers have analyzed or reviewed analyses of probably more than 200 specimens of mustards of different species and varieties, and have rarely observed a specimen of clean material yielding over 5 percent of total ash, or over 1 percent of acid-insoluble ash. Commercial methods for cleaning mustard have been so far developed that material may invariably be obtained containing less than these amounts, although the present U. S. Pharmcopoeia standard for both black and white mustard allows 9 percent of total ash. The Department of Agriculture some time ago promulgated a standard of 5 percent total ash for mustard used as a food, and a limit of 1.5 percent of ash insoluble in hydrochloric acid.[4] A few instances have in the meantime come to our attention which suggested that the standard for total ash might be 6 percent rather than 5 percent, in order to cover exceptional cases of naturally high ash in the seed. The standard thus amended, 6 percent for total and 1.5 percent for acid-insoluble ash appears quite satisfactory for mustard used as a drug or as a food.

Rhubarb.—In connection with rhubarb several interesting cases have recently come to light. In one instance a sample of the powdered drug, having been analyzed and found to yield about 20 percent of ash, which of course is far in excess of the U. S. Pharmacopoeia limit of 13 percent, the dealer was cited. It developed in the hearing that the material had been ground from a very fine grade of Shensi rhubarb, the variety most highly prized by the trade. Some of the original whole drug being available, this was submitted to the Department for analysis. The analysis[5] of the sample, which was clean and of excellent appearance, revealed that the material contained about 20 percent of total ash, of which less than one-tenth of 1 percent was insoluble in acid. Rhubarb is known to contain comparatively large amounts of organic acids, especially oxalic in the form of calcium oxalate. It was, therefore, not altogether surprising that a sample which yielded such a high ash should show as well such a low acid-insoluble ash. Since this occurrence several other shipments have been offered for importation which also yielded a total ash in the neighborhood of 20 or 21 percent, although in every instance the acid-insoluble ash was practically negligible. It would appear, therefore, that the present limit of 13 percent total ash for rhubarb should be raised to 22 percent; by including at the same time an acid-insoluble ash standard of 1

[4] *Food Inspection Decision*, 1918, 172. "Condiments other than Vinegar and Salt," par. 33.

[5] Analyst: Mr. Eugene Bloomberg, Buffalo Laboratory, Bureau of Chemistry.

percent, sophistication of a powdered drug normally yielding a low total ash would in a considerable measure be prevented.

Sassafras.—Sassafras is a drug which is altogether of domestic origin, and since facilities for inspection of domestic drugs are not so advantageous as for imported drugs, attention has not heretofore been directed to the present absurd U. S. P. ash standard of 30 percent. Recently, however, analyses[6] of two authentic clean specimens showed a total ash of 2.5 percent and 3.7 percent and an acid-insoluble ash of 0.5 percent and 1.3 percent, respectively. Another sample which yielded a total ash of 18.85 percent showed an acid-insoluble ash of 14.8 percent; the latter consisted very largely of earth and sand. This also was an authentic sample, but was extremely dirty. Other analyses of this product which have been noted in the Bureau, as well as analyses reported in literature, show that it is entirely practicable to obtain commercial material which yields less than 10 percent of total ash and 5 percent of acid-insoluble ash. Even these figures appear far too liberal for a standard.

While the instances cited above by no means exhaust the list of drugs where present standards could be advantageously altered and supplemented by standards for acid-insoluble ash, they include some of the more striking illustrations which have been recently noted.

The effect which the presence of different parts and portions of the plant may have on total ash is discussed above in the case of Hyoscyamus. Newcomb and Rogers[7] also brought this out in the case of Digitalis, and Sievers[8] in the case of Belladonna. It appears to be quite a general rule, observed by other workers as well as ourselves, that the leaves are richer in ash than the stems or flowers, and that the more stems there are present the lower usually will be the ash. This seems to hold true also for the acid-insoluble ash.

The influence which varietal, environmental, and soil conditions in particular may have on the amount and composition of ash has also been previously discussed in the literature. Rogers and Newcomb have recently discussed this in the case of digitalis, and have pointed out that the cultivated forms, on the average, yielded higher amounts of ash than the wild form.[9] We have pointed out above in the case of rhubarb that a high ash is not necessarily an indication of uncleanliness; since rhubarb contains considerable amounts of oxalic acid in a soluble form, it is readily conceivable that in plants grown in calcareous soils the amount of calcium oxalate may be appreciably greater than in plants grown on other soils.

When the pure ash of a vegetable drug is heated with 10 percent hydrochloric acid, only a small portion, as a rule, remains undissolved. From the amount, then, of this acid-insoluble portion of ash one can usually draw a definite conclu-

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[6] Analyst: J. F. Clevenger, this laboratory.

[7] Newcomb, E. L., and Rogers, C. H., "The Relative Activity of Separated Portions of Digitalis," *Amer. Journ. of Pharmacy*, 90, 580–8, 1918.

[8] Sievers, A. F., "The Percentage of Stems on Belladonna Herb and Its Effect on the Quality of the Herb," *Ibid.*, 90, 847, 1918.

[9] Rogers, C. H., and Newcomb, E. L., "A Method for Cleaning Digitalis, with a Study of the Inorganic Constituents," *Ibid.*, 90, 239–252.

sion as to the presence or absence of sand and earthy material in a drug sample.[10] The determination of the amount of acid-insoluble ash present in a drug will therefore be valuable as a test for purity. It requires very little more time than the ash determinations, and is, as we have seen, sometimes of even more value than the latter in the final judgment of cleanliness. The addition of an acid-insoluble ash standard will permit the raising of the total ash standard of a number of drugs, such as rhubarb, mentioned above, in order to cover wide variations due, probably, in the main, to soil conditions, and at the same time guard against careless handling or gross adulteration of drugs both in the whole and particularly in the powdered form.

The following simple method has been followed by the writers for a number of years:[11]

To the ash obtained by the U. S. Pharmacopoeia method is added 25 Cc. of 10 percent hydrochloric acid. This is digested on a steam bath for about 10 minutes, filtered, washed, ignited over a bunsen burner, cooled, and weighed.

While it is well known that a certain amount of siliceous matter can only be rendered insoluble in hydrochloric acid by several evaporations to dryness, the method as given approximates that given for the determination of ash insoluble in acid in the Bureau of Chemistry Bulletin 107, Revised (1912), page 162, under "Methods for the Analysis of Spices," and is sufficiently accurate for purposes of crude drug control.

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ON THE SHRINKAGE OF ALCOHOL-WATER MIXTURES.

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The United States Pharmacopoeia states that when 500 mils of alcohol are mixed with 500 mils of water "if the two liquids are measured at the temperature of 25° C, the mixture when cooled to the same temperature will measure about 970 mils." In some experiments which I have been engaged in, it was important to know what volume percentage of alcohol would result from mixing alcohol of a given strength with water. It is evident that a mixture, for example, of equal volumes of absolute

[10] Fortunately the dust, dirt, and sand often adhering to drugs after collection can, to a considerable degree, be removed, even if the drugs are in the dried condition. Rogers and Newcomb (*loc. cit.*) have shown this in the case of digitalis, and we also have had similar experience with other drugs (mustard, for example). The importance and feasibility of cleaning drugs, however, appears to be not so widely recognized as it should be. The more the machines and methods used in the grain and related industries are applied to the cleaning of drugs and spices, the less difficulty will the trade experience in obtaining high grade products.

[11] To demonstrate the presence of sand and dirt directly in a powdered drug, without an ash analysis or microscopic examination, we have in a few instances floated the material on carbon tetrachloride, a liquid of high specific gravity (1.630). The vegetable matter usually floated on the surface, while the mineral impurities sank to the bottom. A very dirty commercial sample of Pennyroyal leaves so treated yielded a precipitate which, when dried, amounted to 26.7 percent while an acid-insoluble ash determination gave 27.9 percent, the two results being in surprisingly close agreement.