ON THE SAMPLING OF CRUDE DRUG.*

BY A. JOHN SCHWARZ.

The problem of sampling crude drug, in order to obtain an official sample, is much more difficult than it is usually believed to be by those who have not come in contact with this phase of drug work. With but few exceptions no two lots of drug are ever received in duplicate conditions. Local collectors, after having cured the drug, pack it loosely in burlap bags; at the collecting centers the cured drug is usually baled before it is sent into market. Adulterations can be more cleverly covered in baled drug than in those cases where drug is packed into bags with foot pressure. Drug should be examined macroscopically and, whenever necessary, followed by microscopical examination, to establish its identity. The amount of foreign material, both organic and inorganic, should be determined and checked up against the standard requirements.

Root bark should be examined for presence of stem bark; leaves, fruits and seeds should be examined for excess presence of stem material, and so on—each shipment should be examined through it's official sample to determine whether or not it comes within the limitations of the official definition.

But what is the official sample? At this point we seem to run into difficulty. It is the opinion of one group that sampling should be carried out on a percentage basis; that is, 10% of a shipment, according to their plan, would be inspected and the conclusions for the whole lot would be based on that portion. This is interpreted that in the case of a 50 bag shipment, only five bags would be inspected. Personally I am opposed to such a plan, and, I feel reasonably sure that I have followers who agree with me that every bag, bale, box or barrel of drug should be examined and passed upon for its identity. This principle, I believe, is held by manufacturing pharmacists. My experience as pharmacognosist has conclusively proven this factor to me. It is not a common occurrence, but occasionally a bag of foreign drug will be received as part of a labeled shipment. I am satisfied that this is not a willful adulteration in all cases, as it is incredible that a drug collector would adulterate low priced drug with a more expensive article. Such cases as have come to my notice within the past year are Bloodroot in a Mandrake shipment; Serpentaria in Blue Cohosh; Veratrum in Black Hellebore; Pink Root in Serpentaria. It is true that in most cases the error would be checked up by the drug miller, but if an inexperienced miller would grind a 5 bag shipment of Serpentaria containing one bag of Pink Root, it is not difficult to imagine the Pink Root going through the mill undetected. Also, for apparently no reason other than adulteration there are times when a bag or two of dirty or unwashed roots appear in a shipment of clean roots. By the percentage method of inspection, bags of this type might be missed, which when ground up with the shipment, would greatly increase the percentage of inert foreign material, thereby reducing the therapeutic value of the entire shipment.

The first step toward getting the official sample is getting a composite sample. This sample consists of a portion of drug obtained from various parts of each container in the shipment. This sort of sampling will be greatly affected by the

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size of the shipment. A shipment of a few bags will receive closer inspection than carload lots. This expression probably calls for an explanation. Let me make myself clear by citing my routine method of inspecting drug. Shipments of 10 bags or less are sampled from the top, bottom and side. Larger shipments than these are inspected by sampling the top and side of one bag, bottom and side of another, top and side of the third and so on. In handling carload lots, inspection consists of sampling the top of bag No. 1, the side of bag No. 2, the bottom of bag No. 3, the side of bag No. 4, the top of bag No. 5, and so on. This procedure is followed if the general run of the drug is uniform. If any one or more bags stand out as being decidedly different, an individual sample is taken and set aside for special study.

After the composite sample has been obtained by the above method, it is necessary to reduce it to the working sample, which, of course, turns out to be the official sample. This is obtained by using the quartering principle. The composite sample, after having been thoroughly mixed and sifted to remove sand and fine dirt as well as broken pieces of drug, is divided into four equal portions. One of these quarters is then taken and again divided into four parts. This is continued until one of the quarters is reduced to working size, or one pound for each thousand pounds or less of drug which it represents. In choosing the final quarter a more representative sample may be obtained by taking one half of two opposite final quarters and combining them. The portion of dirt, sand and broken pieces of drug which were sifted out is now quartered on the same plan as that just described. The final quarter of this is then added to the final quarter of the above which then constitutes an official sample.

Drug, for the purpose of sampling, can be divided into two classes, that of which the component parts have a diameter greater than 1 cm. and less than 1 cm. Drug which has a diameter of less than 1 cm. is sampled by means of a sampler of the type used in the cereal industry for grain sampling, whereby a core of the drug is removed. This class would include small seeds and fruits, trichomes, spores, etc. There is no doubt that this produces a uniform representative sample. This sort of sampling must be resorted to rather than the method employed for sampling the other class of drug. The difficulty in this class is due to the fact that when the container is punctured the drug pours out.

In sampling the drug of larger diameter than the above, the container is sliced at various points as has been mentioned when treating of the manner in which the official sample is obtained. It might be well to consider a few special points in sampling drug of this class. First, we have roots, which, when badly intermingled, are best sampled by use of a hook. Drug treated in this way would include Gelsemium, Sarsaparilla, Asparagus Root, Hydrangea, Licorice Root, Queen of the Meadow, Culver's Root, and many other similar drugs. There is much danger of obtaining an unrepresentative sample due to the fact that when these roots are pulled out much of the silica and fine dirt is brushed off.

Second, there are the barks with which we have similar difficulty; these are Cotton Root Bark, Blackberry Bark and the like.

Third, the leaves, particularly those in baled lots, which have been packed before they are thoroughly dried, give us considerable trouble. It is important that we obtain samples from the center of the bale. Everyone realizes the diffi-

culty encountered in splitting bales because of the subsequent difficulty in storing or rebaling. Yet an article by B. Pater, the abstract of which appeared in the *Pharmazeutische Zeitung*, proves conclusively that such a procedure should be followed. He tells of the alkaloidal content of mildewed Hyoscyamus leaves being reduced to one-half of the normal content. Leaves which are packed before being thoroughly cured are very susceptible to mildew. Baled drug, which has not been sufficiently dried, receives enough of an air current through the surface portion of the bale to prevent any mildew formation and for this reason when a sample is taken only from the exterior portion of the bale, the assay result would classify it as normal drug. But upon grinding the bale and assaying a sample of the ground drug, the alkaloidal strength would show up as approximately half standard. While Pater's work has been confined only to Hyoscyamus, there is no reason for believing that other drugs do not undergo similar decomposition of their constituents under similar conditions.

As stated before, every one of you is probably aware of the difficulties encountered in drug sampling. You are perhaps likewise aware of the fact that there are as many methods employed in sampling drug as there are people engaged in this line of work. This fact was probably best brought home to those present at the Plant Science Seminar conducted at the University of Minnesota this past summer. Several experiments were carried out on ash determinations as well as alkaloidal determinations in which two or more people were asked to obtain a sample from the same lot of drug. In no two cases did the samples check up satisfactorily, especially in the case of the ash determinations.

I feel confident that all houses engaged in the manufacture of pharmaceuticals will agree that the foregoing method is the most satisfactory for obtaining authentic representative samples. The percentage method of inspection may be used to advantage by government representatives in their inspection of imported drugs, and also by those houses dealing only with the collection and distribution of crude drugs. However, pharmaceutical manufacturing houses cannot afford to put their well-established reputations at stake when the question of authentically identifying crude drug is based upon the percentage method of inspection, and consequently I feel that the above method should be given due consideration when the definition for obtaining an official sample is formulated.

DEPARTMENT OF PHARMACOGNOSY,
ELI LILLY & COMPANY, INDIANAPOLIS, IND.

DISCUSSION.

CHAIRMAN COOK: Could not some machine be devised with a cylindrical cutter that would remove a core from a bale of compressed leaves or flowers or similar drug which could be laid out in a trough so that the sample would show the drug in the order in which it was placed in the bale?

MR. SCHWARZ: Such a scheme has been worked with Scopola, and such a sample might well be designated the official sample. I am quite confident that within the next few years a machine for very rapidly boring bales will be on the market and used for sampling every bale of a shipment.

MR. GLYCART: I wish to know what type of mill to use in a laboratory for grinding samples. In the grinding of drug, is not the usual high speed mill liable to develop so much heat as to "burn" the drug and partially destroy the alkaloid? Would a ball mill be better, and is the heat developed as high in grinding with such a mill?

E. L. NEWCOMB: High speed mills will generate heat, and care must be exercised to prevent loss of the active constituent of the drug. In the case of cloves, a special grind is followed to

prevent vaporizing the volatile oil. The deterioration of the alkaloids in Nux Vomica has been noted from grinding the drug very fine in high speed mills. The proper grinding of drugs is one of the great unsolved problems. There is need for a model laboratory mill. If specifications for such a mill could be formulated, there would be no trouble about its manufacture, for it would be in demand. If those who desire such a mill could get together and present their needs to a manufacturer of mills, it might lead to the production of an ideal laboratory mill.

GEORGE D. BEAL: We have been using, at the University of Illinois, a ball mill for grinding inorganic samples. Several times our laboratory man has attempted to grind drug samples, but it has not proved satisfactory. To obtain a fairly uniform sample, frequent sifting is necessary, and this involves much time and attention. Stramonium grinds easily, and Aloe also, if handled right. The ball mill does not heat so rapidly because it grinds more slowly. We have found it useful as a shaker in extraction with immiscible solvents. Even with ether, there is no tendency to emulsification.

CAN THE ANTHRAQUINONE DRUGS BE SCIENTIFICALLY VALUED?*

BY GEORGE D. BEAL.

The quantitative valuation of any substance can only be accomplished when some ONE at least of the following conditions can be satisfied:

1—The constituent must be capable of separation in pure form in such fashion that the usual form of gravimetric determination may be completed.

2—It must undergo some characteristic reaction which may be quantitatively measured.

3—It must have some physical constant which can be quantitatively measured.

4—It must produce some definite and measurable physiological action.

Condition 1 requires that the substance contain some constituent capable of separation unchanged, or as a definite compound, the nature of which may be correlated with the valuable properties the substance is assumed to possess.

Conditions 2 and 3 require that the nature of the constituent be so well known that the physical or chemical constant may be correlated with the composition of the drug.

Condition 4 requires the recognition of some definite physiological property, that this property be the cause of a phenomenon which can be accurately observed and measured, and that this property is so well recognized that a standard can be described in some way for purposes of reference.

The Constitution of the Drugs. It is now definitely known that the characteristic principles which are separated in the course of a laboratory investigation are derivatives of methyl anthraquinones. Evidence points to the existence of these in the drug in part in the free state and in part in a form of combination which is akin to a glucoside.

The glucoside hypothesis is favored for the following reasons. (*a*) Glucoside like derivatives have actually been isolated and on appropriate treatment have yielded a sugar and anthraquinone. (*b*) Prolonged extraction in presence of water and of high temperatures yields an extract from which much larger amounts of free anthraquinone can be separated than when extraction takes place under non-hydrolyzing conditions. (*c*) The action of hydrolyzing agents on the drug or the extract therefrom produces a greatly increased yield of free anthraquinone derivatives.

* Read before the Unofficial Conference of U. S. P. and N. F. Revision Workers at Chicago, January 12, 1924.