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.

Possible Methods of Valuation.—The writer is inclined to discard for the present possible biological methods of assay. The properties do not lend themselves to accurate measurement and the relative effects of the free and conjugated hydroxy methylanthraquinones are not definitely understood.

Chemical Standardization.—The second objection to biological standardization, lack of correlation of composition and properties, is equally applicable here. There are certain factors, however, which can be measured by chemical means.

Tschirch[1] and others have suggested a series of possible methods:

1—A spectroscopic method based on the absorption spectra of the alkali salts of the hydroxymethyl anthraquinones.

2—Colorimetric measurement of the alkali salts.

3—Colorimetric as above but without the colorimeter.

4—Precipitation by coupling with diazotized *p*-nitranilin.

Warin[2] has developed a colorimetric method based upon the reaction with nickel salt and alkali, as used by Beal and Okey[3] in qualitative work.

Daels[4] has used extraction with chloroform, before and after hydrolysis with sulphuric acid, to determine what he designates as "free" and "combined" hydroxymethyl anthraquinones.

Beal and Gunton[5] have, they believe, successfully applied this method in the examination of Frangula, Cascara, Rhubarb and Rumex, both *R. crispus* and *R. ecklonianus.*

Fuller[6] has likewise used it and recommends it for further study by the A.O.A.C. He has used the colorimetric method with less success, and has used the diazonitranilin method for aloin.

Throughout recent literature the sentiment prevails that a very good indication of the extent of the free and combined anthraquinone content may be had by an application of Daels method.

The principal criticism of the colorimetric method is that of all such methods, together with the difficulty of obtaining a standard which will possess the same *color values* as the unknown.

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DISCUSSION.

A. G. DUMEZ: I wonder if the anthraquinones give a true indication of the therapeutic values. I recall a sample of Rhubarb from which the methyanthraquinones had been extracted and yet it still possessed cathartic properties. There are so many possible forms of combination that we hardly know the true therapeutic constituent. The physiological value of the drug bears to some extent a relation to the total amount of the derivatives.

MR. GLYCART: A sample of crude powdered Cascara reported upon some time ago, apparently had depreciated about 50 per cent. in value during a year's time. Is there any explanation of this?

GEO. D. BEAL: It is doubtful if deterioration would occur at this rate. You can hardly find a more stable compound than these anthraquinone derivatives. For example, in my work a

few years ago with Miss Okey, we wished to verify a specimen of emodin by a determination of the carbon and hydrogen content. Following the ordinary combustion procedure, the specimen was burned in an atmosphere of pure oxygen using copper oxide in the combustion tube. The copper oxide was heated to a white heat. Under these conditions, we found an orange-red sublimate in small amount in the absorption train which indicated that a portion of the material had passed over this white hot copper oxide in an atmosphere of pure oxygen and had undergone little, if any, change.

E. L. NEWCOMB: Some one has pointed out that "black hearted" Rhubarb yields a product which contains a larger amount of anthraquinones than does solid fresh rhubarb. There is another point that has not been mentioned heretofore. The astringent properties possessed by Rhubarb bear an important relation to its therapeutic value. Possibly the anthraquinones, glucosidic in nature, are in combination with the tannins. At any rate, no method which measures merely the laxative properties and does not take into consideration the astringent values will fully estimate the value of the drug. The importance of these compounds should be considered in connection with the work on this drug.

E. N. GATHERCOAL: Dr. Beal was asked to present this paper at the Conference because it represents a type of unsolved problem in connection with Pharmacopœial Revision that should be brought to our attention; the problem of the valuation of drugs. Perhaps in Europe and America during the last decade or so, more research work has been done on the determination and estimation of the active principles of the anthraquinone drugs than upon any other drug or group of drugs. Dr. Beal has splendidly presented the problem. Fortunately, the anthraquinone drugs, if properly prepared, are likely to be of uniform quality and are not liable to deteriorate, but rather, perhaps, tend to improve upon aging.

MR. WARREN: Whether the anthraquinone reactions really do evaluate this group of drugs, or even can be relied upon to detect these drugs, is a question that has arisen in connection with certain problems. I recall that at one time, a certain compound medicine was claimed to contain cascara, but I could not, after repeated trial, obtain any identifying reactions. Yet there was no question but that the therapeutic properties fully indicated cascara.

REPORT OF THE SCOVILLE ORGANOLEPTIC METHOD FOR THE VALUATION OF CAPSICUM.*

BY ELMER H. WIRTH AND E. N. GATHERCOAL.

The Scoville Organoleptic Test offers a simple and fairly accurate means of determining the approximate pungency of a given sample of Capsicum. Although it possesses to a certain degree the limitations of all organoleptic tests it may be considered as being of greater value than the average in as much as it depends upon the sensation of pungency rather than on the sense of taste. This greatly eliminates the personal equation so prominent in the great majority of organoleptic tests. Experiments with unknown samples on students show a fairly consistent check as to results and the factor due to personal equation is quite constant.

The test itself as proposed for the U. S. P. is as follows: mix well 1.0 Gm. of the powdered capsicum in 50 cc. of alcohol in a stoppered flask and macerate for 24 hours. Dilute 0.1 cc. of the clear supernatant liquid with 140 cc. of a 10% solution of sugar in distilled water. Five cc. of this solution swallowed at once will produce a distinct sensation of pungency and taste of capsicum in the mouth and throat.

The pungency of capsicum is generally conceded to be due to capsaicin. This test therefore sets a standard for the minimum amount of capsaicin permissible in

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