NOTES ON VARIATIONS IN THE WEIGHTS OF QUININE SULPHATE CAPSULES.*

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There apparently is some confusion in the methods used by various pharmaceutical manufacturers in the weight determinations of quinine sulphate capsules. Different authorities recommend different methods and there is usually no close agreement in the results expressed. In an endeavor to arrive at a more satisfactory method of determination, we have made the following observations for which no claim of completeness is made. We have used machine-filled 5-grain quinine sulphate capsules, made by leading manufacturers and purchased on the open market, for these examinations.

Several factors must be taken into consideration in devising a reasonably accurate method for determining the weights of quinine sulphate in gelatin capsules. First and foremost, as is well known, quinine sulphate is very efflorescent and loses weight in air under ordinary temperature and humidity conditions. Capsules filled with quinine sulphate from a newly opened container will lose more than 5 per cent in weight in 12 hours under similar atmospheric conditions, due entirely to loss of moisture. One hundred ounces of U. S. P. X quinine sulphate from a freshly opened container will lose ten ounces or more of moisture when exposed over night to the air. A group of ten recently filled five-grain capsules, containing no admixed starch, lost 3% in weight in three hours on the laboratory table and when allowed to remain undisturbed over night, the total loss of weight was 6.38%. It can readily be seen that this may lead to serious difficulties when the capsules are officially investigated. The required amount of quinine sulphate is present but, due to loss of moisture, the net weight is low.

This source of trouble can be eliminated by the addition of starch to the air-dried quinine sulphate crystals. The mixture being in fairly good equilibrium with the humidity, little change in weight occurs.

The gelatin shells, if used as counterpoises in assaying the finished product, are also a great source of error; in fact, they are probably the source of greatest error. These empty capsules change weight quite rapidly as the humidity varies, taking up and giving off moisture; this will account for a small error.

The weight per empty shell varies greatly from the average weight of a number of them; the lightest and the heaviest shells in a large group weighed individually, varied 13.6% from the average weight (1.54 grains each) of that group. It is our understanding that this particular variation in weight is unavoidable in the manufacturing process. This comparatively great variation in weights militates against using a single capsule at any time as a counterpoise in arriving at the correct figure for the net weight of any one capsule.

One of the largest manufacturers of quinine sulphate capsules determines the weight of his product by carefully emptying the contents of each capsule on to the pan of an analytical balance and thus arrives at the net weight of the contents.[1] This, of course, would be an ideal method, and is undoubtedly quite accurate, but it has been our experience that it is somewhat difficult to absolutely empty, com-

* Section on Practical Pharmacy and Dispensing, A. PH. A., Toronto meeting, 1932.

[1] Private communication.

pletely, the contents of the capsule. Quite frequently an appreciable quantity of the sulphate remains clinging to the interior surfaces of the capsules, in spite of efforts made to remove all of it. The error from this source may be quite large.

An additional failing of this method is the fact that comparatively few capsules from a large lot are actually weighed; too long a time is required to completely empty a hundred or more capsules and weigh the contents.

One authority weighs each capsule individually, using a single empty shell as a counterpoise. We have found that while this method usually gives results which closely approximate those obtained by the method recommended in this article, there are, nevertheless, variations. We believe these differences to be due to the variations in weights of the empty shells used as counterbalances, which have previously been described. As an example of this, one capsule weighed 5.11 grains net with a certain empty shell, while the same capsule weighed 4.97 grains with another empty shell of the same lot. This is a variation of nearly 3% due entirely to the counterpoise weight.

Of course, for accuracy and for a real "umpire method" the weights may be determined in the usual way, by shaking out the quinine with chloroform; this, however, requires time, and is to be avoided when possible.

During the course of these brief experiments there were noted several rather large variations in the actual sulphate content in a single lot of capsules. For instance, in a lot produced by one of the largest manufacturers, one capsule had a net sulphate weight of 84.4% of standard, and another from the same bottle weighed 124.2%; this is the weight of quinine sulphate alone. These are, of course machine-filled with a quinine sulphate-starch mixture.

As a result of the observations noted, we submit the following scheme for determining the weight of quinine sulphate capsules. This method has been in use in this laboratory for several years and has been found, we believe, to be not only quite accurate, but also reasonably rapid. It has the advantages of the use of many capsules from the large lot being determined and also the use of many empty shells as counterpoises, in order to average the weights of both. The method we propose is to sample as accurately as possible the entire lot of capsules, being very careful to obtain an average sample. The lot may be sampled by the "quartering" method, by passing the whole lot repeatedly through a sampler or in any other suitable way. These capsules are weighed in the laboratory on the balance in groups of 20 against a counterpoise of 20 new empty shells from the same lot as that from which the filled capsules were made, until 200 capsules have been weighed. The 20 empty counterpoise shells are changed completely three times during the weighing of the 200 capsules—to eliminate, as far as possible, the errors caused by abnormal shells. The average weight reported for the entire lot is the figure obtained by averaging these 10 weighings.

CONCLUSION.

We believe this to be as accurate and satisfactory a method for weighing large lots of quinine sulphate capsules as any we have so far studied.

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