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THE QUALITY OF COMPRESSED TABLETS, PARTICULARLY AS TO SOLUBILITY AND EASE OF DISINTEGRATION.*

BY WILLIAM J. HUSA.**

In judging the quality of a batch of compressed tablets there are a number of points to consider, *i. e.*, uniformity of appearance, uniformity of weight, uniformity and accuracy in amount of drug, purity of materials, absence of crumbling, chipping and discoloration, and solubility or property of disintegrating when dropped into water.

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The National Formulary (1) states that compressed tablets composed of insoluble medicaments should disintegrate within a few minutes when dropped into water. In throat tablets, where a continued local effect is sought, the tablets should disintegrate very slowly; while in hypodermic tablets very rapid solution is necessary. Obviously, a tablet which is swallowed must dissolve or disintegrate within a reasonable time if it is to have any medicinal effect; preferably, in most cases at least, it should readily be dissolved or disintegrated. A tablet that will pass through the alimentary tract without disintegrating is not only useless, it is worse than useless, for it not only fails to have the desired effect, but through the confidence wrongly placed in it, stands in the way of other treatment which might prove beneficial.

The solubility of a tablet depends, to a certain extent, on the solubility of its ingredients. In the case of insoluble substances, the treatment will differ according to whether or not the substance possesses a cellular structure. Vegetable powders, such as ground roots, barks, etc., gradually swell in water; this property assures disintegration of a tablet largely composed of material of this nature. For tablets of insoluble chemicals, something must be done to cause the tablet to disintegrate after it is swallowed. A very common method, of course, is to incorporate 15% or 20% of dry starch in the tablet; when the tablet comes in contact with water the starch swells, thus causing the tablet to break up. According to Scoville (2), such tablets must be kept in well-closed containers, or they will gradually absorb enough moisture to prevent disintegration. Another method is to incorporate a small amount of sodium bicarbonate and citric or tartaric acid in each tablet. When such a tablet is dropped into water, there is an effervescence and the tablet falls apart. Starch may also be used to advantage, in many cases, in the tablet coatings to prevent insolubility due to the coating. Excessive hardness of a tablet, the use of too much gum and the too liberal use of oil as a lubricant are factors which tend to hinder disintegration.

The above facts are well known to tablet makers and it might seem that there is little chance for any trouble due to insoluble tablets. However, Robert C. White (3) has stated that some coatings on the market render a tablet absolutely insoluble and therefore defeat the entire plan of medication. Other investigators (4) have also reported similar results. Henry J. Goeckel (5) has reported a case in which salol tablets passed through the alimentary canal unchanged.

Since tablets which will not dissolve or disintegrate are thus occasionally encountered, it seems to me that there is a chance for the retail pharmacist to do a real professional service by occasionally checking up on the tablets that he buys and dispenses. The simplest procedure is to drop the tablet into a vessel of water and note the result.

I recently made a test of this kind on tablets purchased from an ordinary drug-store stock. I obtained 20 samples of tablets, which included the products of 13 different manufacturers. The tablets were dropped into water at about 80° F. and the results were noted. Some kinds of tablets disintegrated in a few seconds, while two kinds were not disintegrated after two days.

In considering the results, it will be convenient to classify the tablets into groups. Of the synthetic organic chemical tablets tested, 5 kinds disintegrated in 15 seconds or less, one required about 1 minute and two required about 10 minutes.

Salol tablets (5 grain) did not disintegrate in 48 hours in either water or dilute sodium carbonate solution. One brand of barbital tablets disintegrated in 10 or 12 seconds, while another brand was not completely disintegrated in 10 minutes. Tests with iodine indicated that starch or dextrin was the disintegrator used for this group of tablets. The salol tablets contained starch, but for some reason this was not effective in bringing about disintegration.

Two brands of urotropin tablets were tested; these dissolved without disintegration within 10 minutes. Urotropin tablets are an example of tablets made from a soluble chemical, in which case no disintegrator is required. Tests with iodine indicated that starch and dextrin were absent in the tablets tested.

When tablets of calomel and rhubarb were dropped into water, surface disintegration began after 10 seconds; the tablets were about one-half disintegrated after 5 minutes and completely disintegrated in 25 minutes. A test with iodine indicated that starch and dextrin were absent. The tablet of calomel and rhubarb illustrates the class in which disintegration is brought about by the swelling or the vegetable drug present.

Tablets of whole ovary and thyroid tablets softened up and broke apart in about an hour. An old enzyme tablet which had been in stock for some years had not disintegrated when the experiment was discontinued after two days.

Tests were not made with coated tablets but from the references cited, it would be very desirable to make occasional tests of such products at the prescription counter. The pharmacist will thus be able to eliminate any tablets which were improperly made, or which have lost their power of disintegration while on the shelf. Traveling salesmen who extol the value of their tablets in general terms should be asked to demonstrate the disintegrating power of their tablets.

In regard to salol tablets, it is of interest to note that several years ago the Committee on diluents and excipients of the American Drug Manufacturers' Association (6) reported that the amount of excipient used varied greatly among the different makers. Thus data secured from 12 firms making five-grain salol tablets showed that the percentage of excipient calculated upon the weight of the salol varied from 18% to 65%. This state of affairs emphasizes the fact that compressed tablets have not been standardized by the U. S. P. and N. F. in the manner that other types of preparations such as fluidextracts have been standardized. No standard being set, each manufacturer must chart his own course and, accordingly, it is not difficult to understand why there is sometimes a great difference in the solubility of tablets made by the different manufacturers. In view of the great difference in amount of excipient used by different manufacturers, with resulting differences in the properties of the tablets, it is important that retail pharmacists should become more discriminating as to the quality of the tablets they purchase. The extra care exercised by the pharmacist will bring benefits to the patient, to the physician and to the pharmacist himself, as well as to those manufacturers who are producing superior products.

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THE DETERMINATION OF SUGAR, URIC ACID, UREA AND CREATININE IN ONE CUBIC CENTIMETER OF BLOOD.*

Byrd determines sugar in one drop of blood—this working with a small amount of blood prompted the writer to prepare this paper.

BY EDWARD S. ROSE.

This paper is written with the hope that it may be of interest to those pharmacies doing diagnostic work.

Much progress has been made in the chemical analysis of blood. Such workers as Folin, Benedict, Meyer, Wu, Van Slyke, Cullen, Marshall and others have given dependable methods for determining non-protein nitrogen, creatinine, creatin, urea, uric acid, sugar, chlorides, cholesterol, etc.

Of these many constituents in the blood probably the sugar content is the most important clinically to the average physician in his daily practice. Of the nitrogenous constituents probably the knowledge of the content of uric acid, urea and creatinine in the order named is of the greatest diagnostic value. Knowledge of the other constituents are of value to the physician at times.

Byrd (*J. Lab. Clin. Med.*, 11, 67–75 (1925)) has adapted the Folin-Wu method to the estimation of sugar in one drop of blood. This work suggested to the writer the possibility of determining the above-mentioned constituents in a small amount of blood as one cubic centimeter.

The materials used in the experimental work were solutions of varying proportions of dextrose, urea, uric acid and creatinine, and blood which for the most part was from the chicken.

The scheme of analysis follows that of Folin-Wu. One cubic centimeter of blood, measured in a pipette, is freed of protein in the prescribed manner. In order to obtain the maximum volume of filtrate the mixture is filtered with the aid of a filter pump. This filtrate is used in the following determinations:

Sugar is determined in one cubic centimeter of the filtrate by the Folin-Wu method using Folin-Wu sugar tubes. Prepare at least two tubes of standard sugar solution containing 0.1 and 0.2 mg. dextrose, using for comparison the one nearest the sample. Dilute all tubes to 25-cubic centimeters.

Uric Acid is determined in 2 cc. of the filtrate by the Folin-Wu method with slight modification. In order to match the colors better 1 cc. of the diluted uric acid standard solution is added to the sample and the proper correction made in the calculation. For the comparison at least two tubes containing 2 and 4 cc. of

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* Scientific Section, A. PH. A., St. Louis meeting, 1927.