Assay of Sulfanilamide in Tablets

*By W. E. Honsinger and R. E. Schoetzow**

In the control testing of uncoated sulfanilamide tablets, made with the usual excipients, it is necessary that the sulfanilamide content be determined, and for that purpose it is desirable that a method be used which results in the isolation of the sulfanilamide so that its purity and identity can be demonstrated by means of the melting point. This also serves to confirm the correctness of the assay, at least that it is not too high since, if so, a low melting point would result.

Difficulty was encountered in the isolation of sulfanilamide from tablets by the use of solvents. Sulfanilamide is only very slightly soluble in ether, chloroform or ethylene dichloride, and it is difficultly soluble in petroleum ether and benzene. It is soluble in acids and bases, but cannot be separated from alkaline or acid solution by ether or chloroform. It is more soluble in ethyl alcohol and methyl alcohol. Attempts to take advantage of this fact by using a mixture of alcohol and chloroform to extract the sulfanilamide from a watery suspension of sulfanilamide and the tablet excipients failed to yield pure sulfanilamide. Extraction of the dry powder with alcohol alone likewise resulted in assay residues of low melting point. When these residues were washed with an ice-cold, saturated aqueous solution of sulfanilamide, residues of the proper melting point were obtained, but the residues were lower than theory in weight. It was finally found that if the dry mixture of sulfanilamide and tablet excipients was first freed of soluble material other than sulfanilamide by extraction with a cold, saturated aqueous solution of sulfanilamide and then the sulfanilamide recovered from the residue by extraction with hot alcohol an assay residue could be recovered from the alcohol solution which is close to the proper weight and melting point.

* Analytical Department of the Chemical and Pharmaceutical Laboratories, E. R. Squibb & Sons, Brooklyn, N. Y.

EXPERIMENTAL

The method finally adopted and used with success in the quantitative determination of sulfanilamide in tablets is as follows:

Accurately weigh 20 tablets on counterpoised watch-glasses with an analytical balance, transfer them to a clean mortar, and powder. Accurately weigh 0.4 Gm. of the powder with an analytical balance and transfer it to a 25-cc. glass-stoppered graduated cylinder. Add 10 cc. of an ice-cold, filtered, saturated solution of sulfanilamide. Shake well. Filter through a Jena glass filter (fritted glass filter). Wash any residue in the cylinder and the material on the filter with a few drops of ice-cold distilled water to displace any sulfanilamide solution. Completely extract the residue in the cylinder and the material on the filter with 80 to 100 cc. of hot alcohol. Wash the funnel tip and any exposed edges with a few cc. of hot alcohol. Collect the alcohol and washings in a tared, 250-cc. beaker. Carefully evaporate the alcohol on a steam-bath. Dry in the oven at 80° C. to constant weight. The weight of the residue so obtained must correspond to not less than 92 and not more than 108 per cent of theory (5-gr. tablet).

Determine the melting point of the assay residue by the U. S. P. XI method. This must be not less than 163° C. and not more than 167° C.

The following table gives the results of assays and the melting points of the assay residues on ten samples of 5-gr. tablets:

Melting Point of Assay Residue

Assay, Per Cent of Theory	Melting Point of Assay Residue
95.47	163.3–164.4° C.
93.09	164.3–164.8° C.
98.37	164.0–164.7° C.
93.09	163.5–164.6° C.
98.77	163.4° C.
96.92	164.9–165.9° C.
92.33	165.0–165.7° C.
101.24	164.4–164.9° C.
99.06	163.0–164.0° C.
93.29	164.5–165.5° C.

SUMMARY

A method for the assay of sulfanilamide in uncoated tablets has been presented, in which the purity of the isolated sulfanilamide is shown by its melting point. We suggest that in the development of assays of medicinal substances the assay should, if possible, be such that it will result in the isolation of the active principle and the purity of which can be determined by a melting-point determination or other suitable test.