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Detection and Determination of Chrysotile in Talc USP

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Abstract □ A procedure for the determination of chrysotile in talc was developed. It depends on the adsorption of a sulfonphthalein dye by chrysotile but not by talc. The final measurement is a spectrophotometric determination of the dye left in solution after the adsorption step.

Keyphrases □ Chrysotile—determination in talc USP □ Talc USP—determination of chrysotile as impurity

The wide use of talc as a dusting powder and as a diluent in capsule contents has caused concern about possible impurities, especially asbestos, in the talc. Cralley *et al.* (1) found asbestos in some cosmetic talcs, and asbestos in talc was implicated as a cause of stomach cancer in Japan (2).

Talc, a hydrated magnesium silicate, may ideally be represented as $Mg_3(OH)_2Si_4O_{10}$. It may be contaminated with other minerals such as quartz, dolomite, chlorite, and the various forms of asbestos. Of the asbestos minerals, chrysotile is currently of most physiological concern. Chrysotile, also a hydrated magnesium silicate, may ideally be represented as $Mg_6(OH)_8Si_4O_{10}$. The structure of both minerals is apparently made up of sheets of silicon and oxygen atoms interspersed with sheets of magnesium and oxygen atoms, the difference being in the added magnesium and oxygen in the chrysotile structure.

USP XVIII (3) is rather vague about the chemistry of talc and apparently would admit a talc containing some chlorite. The concern is for rather gross impurities such as excesses of pH or water-soluble iron. Thus, a rather substantial contamination of the talc with chrysotile could occur, and no cause for rejection would appear unless the product became gritty.

Several tests can be proposed to detect the chrysotile in talc, but each suffers from some difficulty, all relating to the large ratio of talc to chrysotile which should be present. Obviously, a simple determination of magnesium, hoping to find the excess due to the chrysotile, would fail because of the natural variability of the talc itself. X-ray diffraction, which was used (4) very elegantly for measuring air pollution by chrysotile, becomes uncertain at low percentages when much talc is present. Optical microscopic examination suffers because the particles approach the limit of resolution of the instrument.

The test described here detects chrysotile contamination in talc but not the amphibole types of asbestos such as tremolite. The test depends on the adsorption of bromcresol purple by chrysotile and the lack of adsorption of that dye by talc. Although other sulfonphthalein dyes of this series have similar behavior, bromcresol purple was selected because of its convenient range for change of color to the acid form.

EXPERIMENTAL

Reagents—Bromcresol purple[1] was used as received. A stock solution of this dye was made by dissolving 0.15 g in 250 ml of 95% ethanol and diluting to 500 ml with water. The working solution was made by taking 20 ml of the stock solution plus 40 ml of 95% ethanol and diluting to 100 ml with pH 4.2 acetate buffer. This working solution, when 10 ml is diluted to 25 ml with pH 4.2 acetate buffer, should have an absorbance of 0.325 at 422 nm.

Chrysotile[2] was used as received except for reduction in particle size to that of the talc being tested.

Procedure—Weigh three 0.2000 ± 0.0010-g samples of talc USP. To Sample 2, add about 3 mg of chrysotile, and to Sample 3, add about 6 mg of chrysotile, both accurately weighed. To each sample, add 10 ml of 50% ethanol–water, and also provide a 10-ml sample of 50% ethanol–water to serve as a blank. Give all samples and the blank an ultrasonic treatment[3] for 2 min at 70 w of power. After the samples cool to room temperature, add 10 ml of working dye solution to each and to the blank. Mix and allow to stand for 30 min with occasional shaking. Then centrifuge the samples and blank, and filter through a 45-μm filter[4]. Dilute a 10-ml aliquot of each filtrate to 25 ml with pH 4.2 acetate buffer. Then determine the optical absorbance at 422 nm in a suitable spectrophotometer, and plot the absorbance against milligrams of chrysotile added (Fig. 1). By extrapolation to a baseline, the level of which is indicated by the blank, the chrysotile content of the talc may be determined.

RESULTS AND DISCUSSION

The assay design used here follows that used for an X-ray diffraction determination of chrysotile in air pollution studies (4). The present design differs in that instead of a positive slope for additions of chrysotile (increased peak height), a negative slope is obtained (increased adsorption and, hence, lower amount of dye remaining). The advantage of using this design is that, in effect, an internal standard is being used which can compensate for variations in the dye used, and it makes a fixed calibration curve unnecessary.

The double-separation step involving centrifugation and filtration was needed because the finest talc and chrysotile particles could not be removed in a reasonable time by centrifugation alone. On the other hand, attempted direct filtration rapidly resulted in a plugged filter before enough filtrate could be collected.

Figure 1 shows a typical determination on a talc spiked with

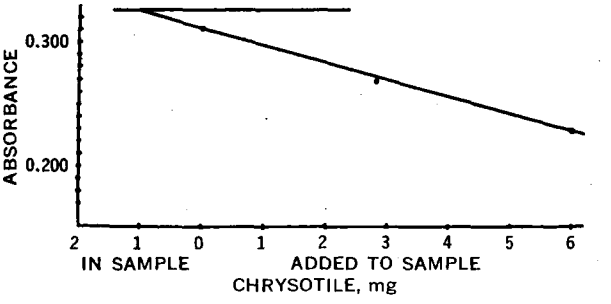


Figure 1—*Extrapolated graph of additions of chrysotile plotted against absorbance.*

[1] Matheson, Coleman and Bell.
[2] Johns Manville Research Center.
[3] Sonifier cell disrupter, model W185D, Heat Systems Ultrasonics, Inc., Plainville, N.Y. The microtip adapter was used.
[4] Millipore.

0.5% chrysotile. The result from the assay in Fig. 1 indicates 1.1 mg chrysotile in a 200-mg sample, or 0.55%. All tests for precision of the assay were done on spiked samples. A limited number of determinations on a sample containing 0.5% chrysotile indicated a standard deviation of ±0.06%.

To eliminate the possibility that a peculiarity of the chrysotile sample used was responsible for the dye adsorption, another sample was obtained[5]. This sample gave substantially the same adsorption behavior as the first chrysotile sample.

SUMMARY

A determination of chrysotile impurity in talc USP was developed. The assay is useful at least at the level of 0.5% chrysotile. An internal standard method is used which eliminates the need for a standard calibration curve. The assay depends on the adsorptive property of the chrysotile for a sulfonphthalein dye.

[5] Geology Department, Indiana University.

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Selective Determination of Phenylpropanolamine Hydrochloride in Pharmaceutical Dosage Forms by Reaction with Ninhydrin

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Abstract □ A colorimetric method for the determination of phenylpropanolamine hydrochloride, based on the reaction with ninhydrin, was applied to various forms of pharmaceutical products. The method is applicable to pharmaceutical products that do not contain other primary or secondary amines. The determination is dependent upon the combined hydroxyl and primary amino moieties. It is postulated that phenylpropanolamine hydrochloride reacts with ninhydrin under the experimental conditions by a mechanism similar to that for amino acids. A comparison of the molar absorptivities of phenylpropanolamine hydrochloride with those of amino acids, such as glycine and phenylalanine, clearly demonstrates the similarity of the reaction mechanism to the classic ninhydrin mechanism.

Keyphrases □ Phenylpropanolamine hydrochloride formulations—colorimetric analysis, ninhydrin reagent □ Colorimetry—analysis, phenylpropanolamine hydrochloride in mixed formulations □ Ninhydrin reagent—used to determine phenylpropanolamine hydrochloride in mixed formulations

In the past few years, phenylpropanolamine hydrochloride has been used widely in many different pharmaceutical preparations as an adrenergic agent. This popularity can be attributed to the fact that it produces vascular and bronchial effects with little, if any, central effects. It is used in asthma and as a nasal decongestant, both locally and orally (1). Phenylpropanolamine hydrochloride can be found in many formulations including tablets, capsules, syrups, elixirs, suspensions, nasal jellies, and nasal solutions.

Recently, because of the increased use of phenylpropanolamine hydrochloride in complex mixtures, it has become necessary to develop a specific and rapid method for its determination. The method described in this report is dependent upon a colorimetric response to concentrations and, therefore, does not require prior separation from other active ingredients present in many allergenic and cold preparations. By contrast, many reported methods require long and tedious separations prior to quantitative determination.

A review of the literature (2–14) showed that a great variety of methods had been used to determine the phenylpropanolamine hydrochloride content in pharmaceutical formulations quantitatively. The methods used were diatomaceous earth[1] separation followed by spectrophotometry, GLC, extraction and titration, anion-exchange chromatography followed by titration with hydrochloric acid, and periodate oxidation to benzaldehyde.

EXPERIMENTAL[2]

Reagents—*Citrate Buffer, pH 5.0*—Dissolve 21.008 g of citric acid USP in 200 ml of water. Add 200 ml of 1.0 *N* sodium hydroxide solution and dilute to 500 ml with distilled water. Adjust the pH with sodium hydroxide or hydrochloric acid, if necessary.

Potassium Cyanide—Accurately weigh 0.1628 g of potassium cyanide, transfer to a 250-ml volumetric flask, and dilute to volume with water.

[1] Celite.

[2] The sample preparation given for layered tablets, capsules, and combination tablets is typical of that required for most dosage forms.