Loss of Fluoride during Tablet Production

Keyphrases □ Fluoride—content in tablets prepared by wet granulation method, effect of processing, dyes, flavors, citric acid, and lubricants □ Tablets—wet granulation preparation, fluoride content, effect of processing, dyes, flavors, citric acid, and lubricants □ Dosage forms—tablets, wet granulation preparation, fluoride content, effect of processing, dyes, flavors, citric acid, and lubricants

To the Editor:

In response to a request from the College of Dentistry of the University of Iowa, colored and flavored chewable tablets containing 0.25, 0.50, and 1.00 mg of fluoride ion were designed and manufactured in lots of 10,000. Since most commercial fluoride tablets are small (approximately 100 mg), the concept was to design large, hard tablets that would require a strong bite followed by chewing to crush them and concomitantly to impact particles into the crevices of the teeth. Therefore, the fluoride would be available in the oral cavity for a longer time than is provided by a conventional tablet that is swallowed intact. To enhance chewing and appeal, flavors and colors were added.

After preliminary formulation, a 600-mg cherry-flavored tablet containing 1.0 mg of fluoride was selected for evaluation. The tablets were prepared by the wet granulation method. Mannitol, sodium fluoride, and saccharin sodium were blended in a twin-shell blender[1], granulated with a gelatin solution, and passed through a mill[2]. The wet granulation was dried in an oven[3] at 50° for 6 hr, and the dried granulation then was passed through a mill[2].

Magnesium stearate, colloidal silica[4], spray-dried stearic acid, and commercial flavor were blended with the dry granulation. Tablets were prepared with a single-punch tablet machine[5] and compressed to a hardness of 20 ± 1 kg using a 1.27-cm punch and die set. The fluoride content was within compendial specifications as assayed by the USP method (1) and the method of Daines and Morse (2).

By using this basic formulation, tablets with other flavors and dyes were prepared and then evaluated by a panel of children[6]. Because orange and lemon-lime were the most popular flavors, orange tablets containing 0.25 mg of fluoride and lemon-lime tablets containing 0.50 mg of fluoride were prepared in developmental lots of 10,000. Although operational and physical characteristics were satisfactory, analysis showed that these tablets contained less than 50% of the intended amount of fluoride.

Since the three formulations were similar except for the dyes, flavors, and flavor enhancer (citric acid), solutions were prepared of all three formulations and of each formulation omitting singularly the dye, flavor, citric acid, magnesium stearate, stearic acid, or colloidal silica. Analysis by specific ion electrode and chemical assays showed that the desired amount of fluoride was present in all solutions.

To determine the effect of processing on the loss of fluoride, lots of 10,000 tablets were prepared similar to the solutions but omitting singularly the dye, flavor, citric acid, magnesium stearate, stearic acid, or colloidal silica. Samples of the dry blend, the wet granulation, the dried granulation, and the tablets were analyzed. It was found that the dyes, flavors, and lubricants did not affect the fluoride content. All formulations containing citric acid were substandard after drying.

Since the wet granulation containing citric acid had the proper amount of fluoride before drying, it appears that fluoride loss is caused by the loss of hydrogen fluoride formed by the interaction of sodium fluoride and citric acid during the drying cycle. Deletion of citric acid from the formulations eliminated the problem of fluoride loss.

When drying moistened mixtures containing sodium fluoride and citric acid, a mild drying temperature of 50° promotes the loss of fluoride, presumably by loss of hydrogen fluoride vapor.

(1) "The United States Pharmacopeia," 19th rev., Mack Publishing Co., Easton, Pa., 1975, p. 460.

(2) T. L. Daines and K. W. Morse, *J. Chem. Educ.*, **51**, 680(1974).

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Received January 19, 1976.
Accepted for publication March 25, 1976.
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[1] Patterson-Kelly Co.
[2] Fitzpatrick comminuting machine model D.
[3] Colton drying cabinet model E.
[4] Cab-O-Sil, G. L. Cabot Corp.
[5] Manesty model F3.
[6] Selected by the Department of Pedodontics.