Preliminary Disintegration Analysis of Commercially Available Multivitamin/Mineral Dietary Supplements in the Adult US Market

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DSID Dietary Supplement Ingredient Database A U.S. Government Initiative

Abstract

An important aspect of dietary supplement evaluation is disintegration, the ability of a tablet to break apart within a specified amount of time so that ingredients are available to the body when needed. As a part of an adult multivitamin/mineral (MVM) study, six (6) tablets from a randomly selected lot per product were sent to a certified laboratory for disintegration analysis (n=94 analyses). Tablets were immersed and agitated in the appropriate media where a visual inspection of the material for all six tablets determined the result. Results were designated as pass or fail according to U.S. Pharmacopeia (USP) disintegration parameters. Products failed the test if >2 of 6 tablets failed to disintegrate in the allotted time or the tablet matrix broke apart too early. Preliminary data received from the laboratory indicates an overall pass rate of 92.6%. Method reproducibility was evaluated using duplicate samples within each analytical batch (n=11 batches). Disintegration information on adult MVMs for the Dietary Supplement Ingredient Database (DSID) will continue to be reviewed and appropriate products will continue to be tested. The DSID project is supported by the Office of Dietary Supplements and the U.S. Department of Agriculture.

Introduction

The Nutrient Data Laboratory (NDL), Beltsville Human Nutrition Research Center (BHNRC), Agricultural Research Service (ARS), USDA, has been working with the Office of Dietary Supplements (ODS), National Institutes of Health (NIH) and other federal agencies to plan and develop a DSID to evaluate dietary supplement products. For the DSID, priority product types and ingredients were identified based on prevalence reports from national surveys where the highest priority product type was adult MVM products (n = 122 products). The DSID is funded, in large part, by the ODS. The major product of this research, the DSID-1, was released in April 2009.

The main objective of the disintegration study was to evaluate disintegration results for adult MVM products. While reviewing the data, factors such as temperature of the disintegration immersion fluid, product form and coating/matrix, and the number of days between purchase date and expiration date were evaluated. Throughout this document, the word 'tablet' includes both product forms 'tablet' and 'capsule' unless otherwise noted.

TABLE 1 – USP 32 Disintegration Method and Immersion Media Information

Dosage Form	Form Preparation	Procedure	Immersion Fluid	Media Temp.	Immersion Time
tablet	uncoated, sublingual	standard disintegration	water	37°C ± 2°C (body temperature-BT)	30 minutes
	coated (plain and film)	standard disintegration	water	37°C ± 2°C	5 minutes at RT then 30 minutes at BT
tablet capsule	delayed-release (enteric-coated)	standard disintegration	simulated gastic fluid (SGF), simulated intestinal fluid (SIF)	37°C ± 2°C	1 hr in SGF then in SIF for the allotted time according to form preparation
capsule	hard gelatin, hard shelled	standard disintegration	acetate buffer (pH 4.5 ± 0.05)	37°C ± 2°C	30 minutes
	soft shelled, soft gelatin (softgels)	rupture	water	N/A	15 minutes

**Information in this table was obtained from USP 32. The equipment used was the Hanson Research QC-21, 2 basket test system (6 tablet capacity per basket).

Materials and Methods

USP chapters <701> (disintegration equipment standards and setup) and <2040> (disintegration test methods for dietary supplements) were followed.

Sample Processing/Testing

1. Each test sample included six (6) tablets from a randomly selected lot of an unexpired product.
2. Samples were repackaged and relabeled (single-blind).
3. Samples were shipped to a certified laboratory in planned batches. Each batch included one randomly selected sample sent as a duplicate to verify method reproducibility.
4. The appropriate immersion fluid and allotted disintegration time (see Table 1) were based on the coating of the tablet (coated or uncoated) or tablet matrix (softgel).
5. Each tablet was placed in a separate transparent receptacle, immersed, and agitated in the appropriate fluid for the allotted time. The temperature of the fluid was monitored and recorded for each tablet in accordance with USP standards (see Table 1).

Pass/Fail Criteria

After a visual inspection of the remaining material, the analyst recorded a 'pass' result if fewer than 2 of the 6 tablets failed to completely disintegrate in the allotted time. According to chapter <701> of the USP, complete disintegration is defined as "*...that state in which any residue of the unit, except fragments of insoluble coating or capsule shell, remaining on the screen of the test apparatus or adhering to the lower surface of the disk, if used, is a soft mass having no palpably firm core.*" (2)

For all tablets, if 1 or 2 of 6 tablets failed to completely disintegrate in the allotted time or in the appropriate immersion fluid, an additional 12 tablets would be sent. For the sample to pass the disintegration test, a total of 16 of 18 tablets must completely disintegrate in the allotted time.

Quality Control

For method reproducibility and as a quality control measure, a randomly selected test sample in each batch (n=11 batches) was sent as a blind duplicate.

Results

A total of 94 analyses were completed (see Figure 1) where the pass rate was 92.6% (n = 87 samples passed). Test results were consistent. For samples that passed the disintegration test, 6 out of 6 (6/6) tablets were reported to have completely disintegrated. For samples that failed, all 6 tablets failed to completely disintegrate. With failed samples, a second lot was sent and again, all tablets failed to completely disintegrate. While reviewing results from the duplicate samples, similar pass/fail results were observed. All 6 tablets in each duplicate sample either completely disintegrated or failed to do so. For retest of the failed duplicate samples, a second lot was sent. Again, all 6 tablets failed to completely disintegrate.

Neither the tablet's coating/matrix nor the temperature of the immersion fluid appeared to predict or determine failure rates (see Table 2). Coated tablets failed about as frequently as uncoated tablets (4 uncoated tablets failed compared to 3 coated). Because of the additional immersion time for coated tablets (see Table 1), it was noteworthy that failure rates for coated and uncoated tablets were comparable. The sublingual tablet and all capsules passed disintegration testing.

Information gathered from this preliminary study will be used to plan and evaluate disintegration testing in future dietary supplement studies.

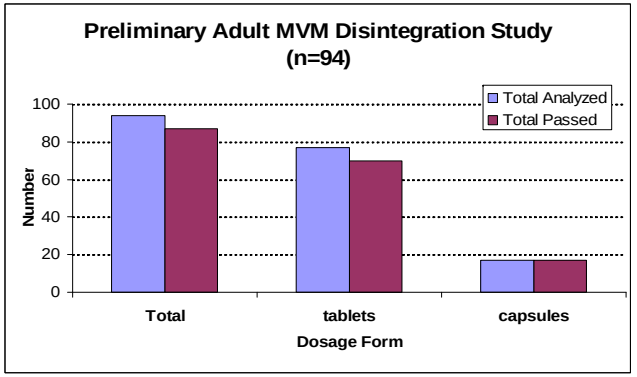

FIGURE 1 – Preliminary Adult MVM Disintegration Study with the total number of samples analyzed and the total number of samples that passed.

Preliminary Conclusions

1. **Approximate 93% of samples tested (87/94) passed disintegration testing**. All capsules (n = 17) passed and 70 out of 77 tablets passed.
2. **The disintegration results were consistent**. For all samples (including duplicate samples), all six tablets either completely disintegrated or failed to completely disintegrate.
3. **After all data was evaluated, the ability to predict disintegration results was inconclusive**. As discussed above, no one factor (or combination of factors) appeared to predict whether a particular sample would pass or fail.

TABLE 2 – Summary of Results by Dosage Form

Dosage Form	Form Preparation	Total Analyzed	Total Passed
tablet	coated	45	42
	uncoated	30	27
	enteric-coated	1	0
	sublingual	1	1
capsule	hard gelatin	12	12
	soft gelatin (softgel)	5	5
Total		94	87

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