

Determination of Calcium Carbonate Content in a Film Coating Using Ultra High Performance Liquid Chromatography-Charged Aerosol Detection

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Introduction

Pigmented film coatings enhance tablet appearance, provide brand differentiation and improve acceptability for consumers. With the increase in consumer preferences for clean label ingredients, calcium carbonate has been evaluated as a replacement of titanium dioxide (TiO₂) as an opacifier in film coating applications. In calcium (Ca) replacement or Ca fortified formulations, it is important to analytically determine the source of Ca in the formulation, i.e. amount contained in the core vs. the amount in the film coating applied. In this study, the calcium carbonate content in the film coating vs. Ca in the core of the formulation was evaluated using a novel analytical test method.

Methods

Three different formulations: (i) oyster shell calcium carbonate caplets (500 mg), (ii) calcium citrate capsules (150 mg) and (iii) placebo tablets were all coated with Nutrafinish®, Dietary Supplement Coating containing calcium carbonate, to a theoretical 3% w/w weight gain. The amount of Ca in the film coating and core was measured by a novel method using an ultra high performance liquid chromatography system coupled with a charged aerosol detector (CAD).

Ca Measurement - Sample Preparation

The samples were prepared using the entire dose, correcting for core content where applicable. The coating was carefully removed and analyzed separately from the core for the caplets (i). For the capsules (ii), the content was removed and only the capsule shells were tested. Samples and standards were diluted with 1% formic acid solution as the diluent to ionize calcium carbonate.

Ca Measurement - Instrument Method

The method used 100 mM ammonium formate as the mobile phase with a flow rate of 0.6 mL/min. Sample and standard solutions (10 µL) were injected at a temperature of 30°C

using a 3.9 × 150 mm IC-Pak M/D column. A linear curve was generated using injection volumes from 1 to 20 µL for quantitation of the Ca ions. The CAD was set with a gain at 2Hz, a filter of 5s and a nebulizer temperature at 50°C.

Results

Assay Results

The sample preparation was developed using component solubility data and the expected concentration of Ca ion. An acidified diluent was selected to ionize calcium carbonate and was also found to be appropriate for calcium citrate present in the capsules.

The presence of Ca in the caplet cores and capsule contents was known to contribute interference to the analysis. This was accounted for by analyzing uncoated caplets, then correcting the coated dosage results using the average uncoated results. The capsules were processed in the same manner, due to the high variability in the fill weights, they did not generate reproducible results. To isolate the coating, the coated capsules were emptied followed by clearing the coated shells of any residue with a dry swab. Analysis of the shells produced recoveries consistent with expected coating weight gains.

The instrument conditions were suitable for all Ca containing solutions. The diluent was compatible with the requirements for charged aerosol detectors.

Chromatographic responses were quantified using calibration curves developed for standards and the limit of quantification was determined to be 5 ppm for calcium carbonate. The linear range of the method was 5 to 100 ppm. Coated and uncoated dosage forms were tested simultaneously to determine the amount of calcium carbonate in the coating vs. the calcium contained in the core for formulations for the calcium carbonate tablets and oyster shell capsules the placebo tablets did not contain Ca.

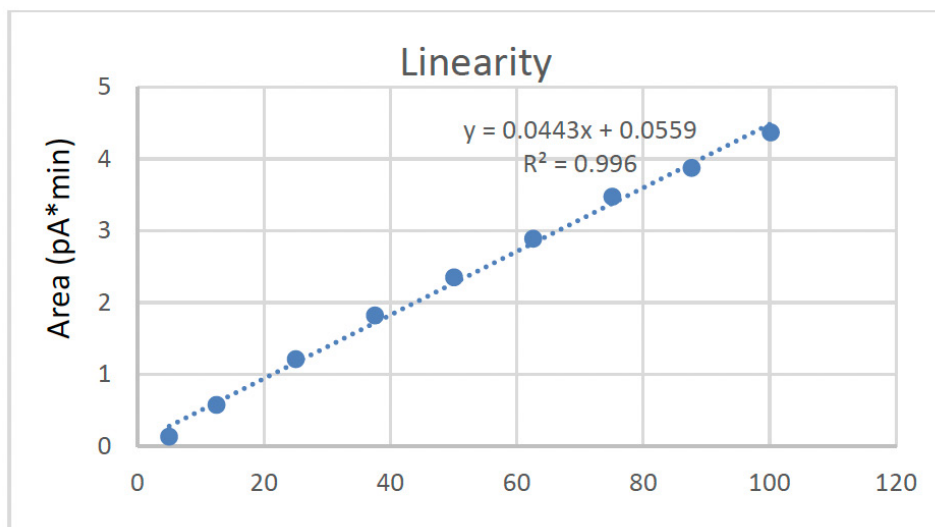
Table 1: Calcium Salt Content of Different Nutrafinish Coated Formulations

Sample	Calcium Core Salt	Calcium Salt Content (mg)			
		Theoretical		Actual	
		Core (mg)	Coating (mg)	Core (mg)	Coating (mg)
Oyster Shell Caplets	Carbonate	750	7.9	755	7.3
Calcium Citrate Capsules	Citrate	622	5.0	668	5.9
Placebo Tablets	N/A	N/A	8.0	N/A	7.6

The calculated and measured amount of Ca in the film coating were similar and the small variations observed were postulated to be due to the differences in coating efficiency of different cores.

Linearity

Figure 1: Linearity of Calcium Standard



The linear range of the method was 5 to 100 ppm. The R^2 value is 0.996 which demonstrates an acceptable linear range.

Precision

Table 2: Precision of Calcium Standard

Injection Number	Calcium	Retention Time (min)	Area (pA*min)	Height (pA)	Tailing
1	Standard	11.308	2.363	5.826	1.20
2	Standard	11.325	2.315	5.820	1.20
3	Standard	11.308	2.392	5.885	1.24
4	Standard	11.317	2.372	5.826	1.20
5	Standard	11.308	2.376	5.961	1.27
6	Standard	11.317	2.329	5.827	1.23
7	Standard	11.333	2.309	5.765	1.21
8	Standard	11.317	2.340	5.746	1.20
9	Standard	11.317	2.375	5.858	1.21
10	Standard	11.317	2.374	5.791	1.20
11	Standard	11.292	2.350	5.774	1.19
12	Standard	11.317	2.321	5.746	1.13
	Average	11.3	2.4	5.8	1.2
	RSD	0.1	1.2	1.1	
	Maximum				1.27

The RSD for the area is less than 2.0% and tailing is not more than 2.0. Both indicate precision reproducibility is acceptable.

Conclusions

A quantification method using ultra high performance liquid chromatography system, coupled with a charged aerosol detector, was developed to determine the content of calcium carbonate in film coatings. The use of calcium carbonate as an opacifier is currently the most effective replacement for titanium dioxide in coating formulations. This work showed a reliable method to quantify calcium carbonate in the core or the coating of coated dosage forms.

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