Dissolution of Glucosamine Veterinary Chewable Tablets Using Ultra High Performance Liquid Chromatography-Charged Aerosol Detection

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Introduction

There has been a surge of interest in natural remedies, vitamins and dietary supplements for animal health products, especially chewable tablets. The matrix composition of a chewable veterinary tablet varies compared to a solid oral dose tablet for humans, and this highlights the need to develop analytical methods that can differentiate between the compound of interest and any interfering component.

The USP Dietary Supplement monograph for glucosamine tablets defines HPLC conditions for assay and dissolution; however, this method may not directly apply to a chewable tablet. These methods employ a C8 or amino phase HPLC column and UV detection at 195 nm wavelength. Analysis at this low wavelength negatively affects the sensitivity and selectivity of the method for impurities in the mobile phase. This is also true from the sample matrix since compounds that are not normally detected at the traditional wavelengths > 210 nm can interfere and increase the baseline noise or produce interfering peaks. For the same reason, differences in tablet formulations could have a dramatic impact on the accuracy of the results determined from this wavelength and impact the robustness of the method conditions. In this study, the dissolution of glucosamine veterinary chewable tablets was evaluated using a novel analytical test method.

Methods

For this study, a veterinary formulation was chosen and different amounts of Starch 1500®, Partially Pregelatinized Maize Starch were used, replacing one or more of the other excipients in the formulation. Direct compression (DC), top spray fluid bed granulation (TS), high shear granulation (HSG) and roller compaction (RC) were used, as methods for manufacturing animal health solid dose products, in this study. Dissolution of each sample was measured by a novel method using an ultra-high performance liquid chromatography (UPLC) system coupled with a charged aerosol detector (CAD).

Glucosamine Tablets Dissolution Set-up

The samples were prepared following the dissolution parameters listed in the Glucosamine Tablets USP monograph: media of 900 mL of water in each vessel, apparatus II paddles rotating at 75 rpm, bath temperature at 37°C, ±2°C, and time point samples at 5, 10, 15, 20, 30, 45 and 60 minutes. The approximate concentration of each sample was 0.33 mg/mL of glucosamine.

Instrument Method (UPLC-CAD)

200 mM ammonium formate, pH 3.65 (20%) and acetonitrile (80%) as the mobile phase with a flow rate of 0.5 mL/min were used. Sample and standard solutions (0.5 µL) were injected at a temperature of 30°C using a 2.1 mm x 100 mm, 1.7 mm HILIC column. The system was calibrated by creating a standard curve from approximately 20 to 140% of the standard concentration, with the target standard concentration of 0.33mg/mL. The CAD was set with a gain at 5Hz, a filter of 10s and a nebulizer temperature at 35°C.

Results

The instruments conditions were suitable for all glucosamine tablet dissolution solutions. All formulations showed consistent dissolution and release of glucosamine from the tablets. The media was compatible with the requirements for charged aerosol detectors.

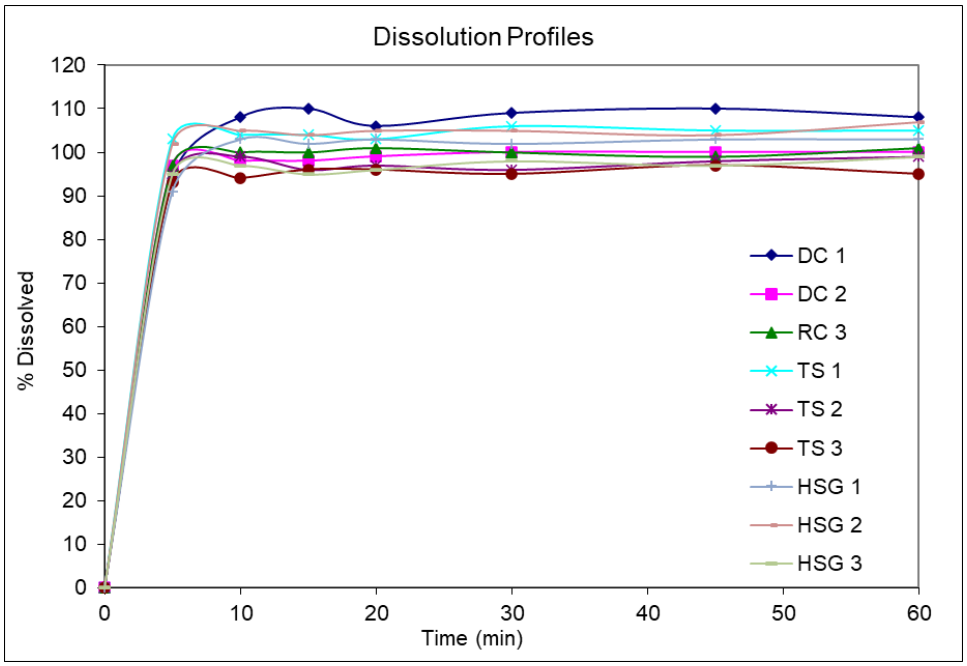
Chromatographic responses were quantified using calibration curves developed for standards and the limit of quantification was determined to be 68 ppm for glucosamine. The linear range of the method was 20 to 140% of the label claim.

The dissolution profiles were all consistent between samples and all fully released by 5 minutes (Figure 1).

Table 1. Samples Tested

Sample No.	Sample Name	Contents
1	DC 1	Glucosamine, Starch 1500, Beet Flavor, Silica, Mag stearate
3	TS 1	
6	HSG 1	
2	DC 2	Glucosamine, Starch 1500, Beet Flavor, Silica, Mag stearate, Microcrystalline cellulose (MCC)
4	TS 2	
7	HSG 2	
5	TS 3	Glucosamine, Starch 1500, Beet Flavor, Silica, Mag stearate, Microcrystalline cellulose (MCC), lactose
8	HSG 3	
9	RC 3	

Figure 1. Dissolution of Glucosamine Tablet Formulations



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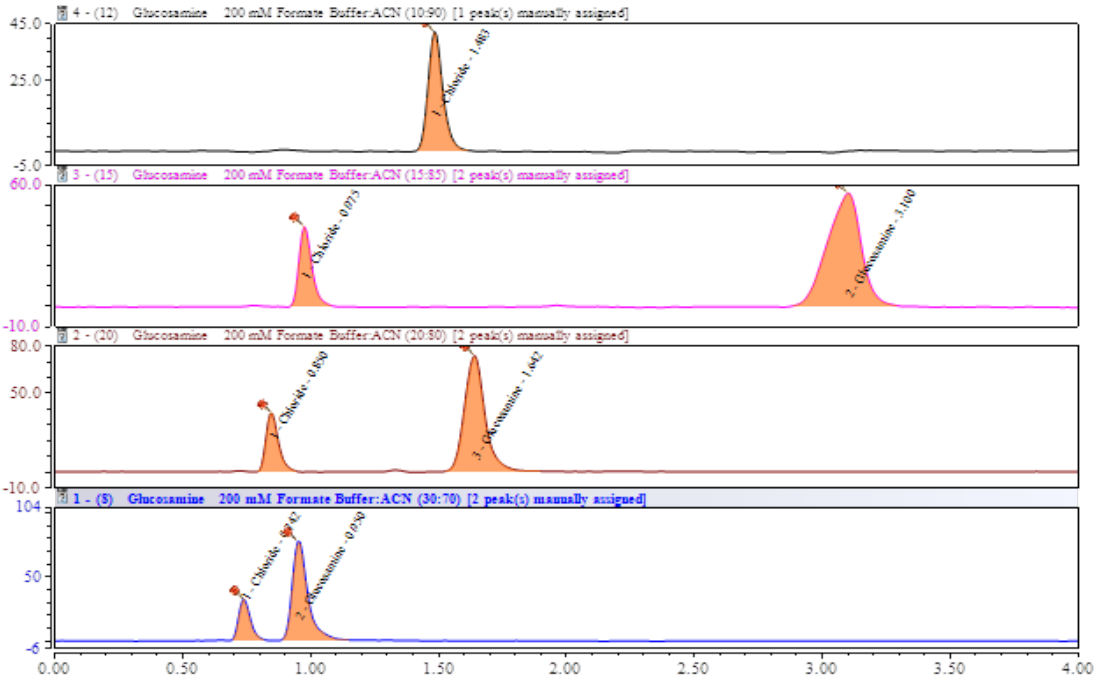
Linearity
The linear range of the method was 68 to 477 ppm. The R2 value is 0.996 which demonstrates an acceptable linear range.

Precision
The RSD for the area of Glucosamine was less than 3.0% and tailing was not more than 2.0. Both indicated that precision and reproducibility were acceptable.

Robustness
The buffer content was varied at different ratios to acetonitrile in order to determine the best separation of the peaks.

Figure 2. Injections of Different Ratios of Buffer to Acetonitrile of the Standard Solution



Conclusions
A dissolution method using ultra high-performance liquid chromatography system, coupled with a charged aerosol detector, was developed for glucosamine veterinary chewable tablets. The use of Starch 1500 with varying excipient combinations in veterinary chewable formulations provided good tablets and excellent release profiles. This work showed a reliable method for dissolution analysis in glucosamine veterinary chewable tablets.

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