Fundamental Evaluation of Moisture Scavenging Property of Partially Pregelatinized Maize Starch using Thermoanalytical Techniques

Raxit Y. Mehta, Manish Ghimire and Ali R. Rajabi-Siahboomi
Colorcon, Inc. Harleysville, PA 19438, USA

AAPS
Poster Reprint 2020

Introduction

Formulation development of moisture-sensitive drugs starts with developing stable and robust core formulation to ensure safety and efficacy over their shelf-life. The selection of suitable core excipients can help to prevent drug exposure to moisture and enhance the stability of the drug product during its shelf-life. Also, the application of a moisture barrier coating and primary packaging is important to limit exposure of the drug to moisture. It has been previously demonstrated that Starch 1500®, partially pregelatinized maize starch has lower water activity compared to the other commonly used excipients.[1] Therefore, its use in the formulation of a moisture sensitive drug can improve drug stability.

The purpose of this work was to investigate moisture interactions of Starch 1500 and microcrystalline cellulose (MCC) using thermogravimetry (TGA) and differential scanning calorimetry (DSC).

Methods

Starch 1500 (Colorcon, USA) and MCC (Avicel, PH-102, Dupont Nutrition and Bioscience, USA) were granulated by addition of 10, 20, or 30% w/w of DI water in a food processor (Cuisinart, USA) for 5 minutes, to ensure uniform water distribution into the excipients. Moisture release rate from 9-11 mg samples was measured at 5°C ramp heating rate up to 300oC using thermogravimetric analysis (TGA Q500, TA Instruments, USA). Differential scanning calorimetry (DSC Q200, TA Instruments, USA) experiments were performed at 5°C ramp rate on cool-heat-cool cycle from 75°C to minus 75°C to identify heat transfers associated with the states of water interaction with the excipients.

Results

Thermogravimetric Analysis

The thermogravimetry technique (TGA instrument, Figure 1) accurately measures the weight loss of the excipient samples, as the temperature of the sample gradually increased. The initial weight loss is due to evaporation of moisture or other volatile components. In this study, TGA was used to measure the moisture evaporation rate of Starch 1500 and MCC at 10, 20 and 30% w/w water levels (Figures 2, 3 and 4 respectively).

a) **Extent of moisture loss at 100°C and 200°C**

Comparing values of weight loss of 20% w/w sample at 100°C and 200°C, weight loss from the MCC sample remained constant (17.5-17.7%), while the Starch 1500 sample kept losing an additional 2.46% w/w moisture over 100°C heating process (Figure 3). A similar trend of continued moisture loss was also observed for 10% w/w and 30% w/w samples of Starch 1500 (Figures 2 & 4).

b) **Rate of moisture evaporation**

The peak moisture evaporation rate of Starch 1500 was 2.20% per min for 20% w/w sample, while 2.71% per min for MCC at the same water level (Figure 3). Lower values of peak moisture evaporation rate for Starch 1500 was also observed at 10% and 30% w/w water levels (Figures 2 & 4). The slower moisture evaporation rate may indicate a stronger association of moisture with Starch 1500.

Peak moisture evaluation rate and extent of moisture evaporation at 100°C and 200°C are summarized in Table 1.

Figure 1: Thermogravimetric Analyzer, TGA Q500

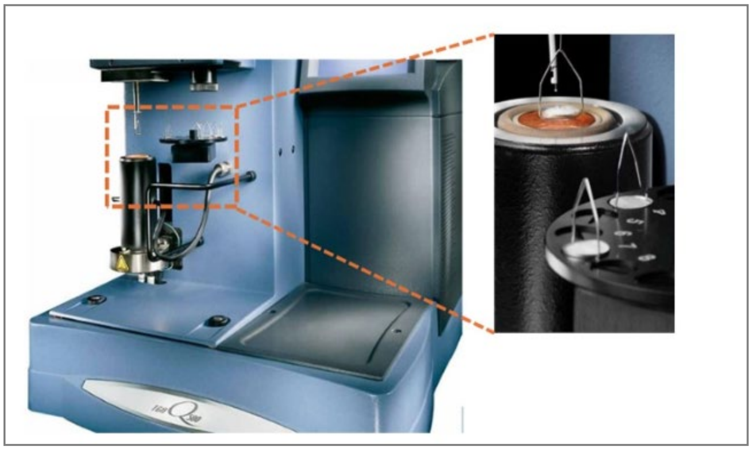


Figure 2: TGA Analysis of Starch 1500 and MCC Samples at 10% w/w Water Level

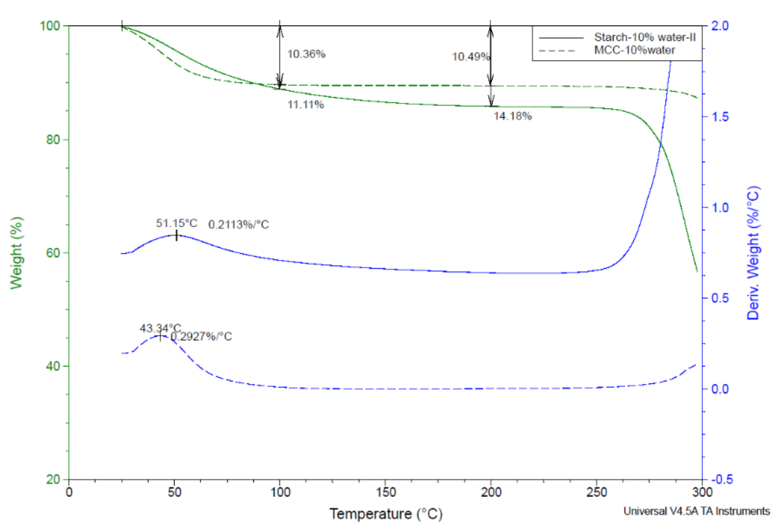


Figure 3: TGA Analysis of Starch 1500 and MCC Samples at 20% w/w Water Level

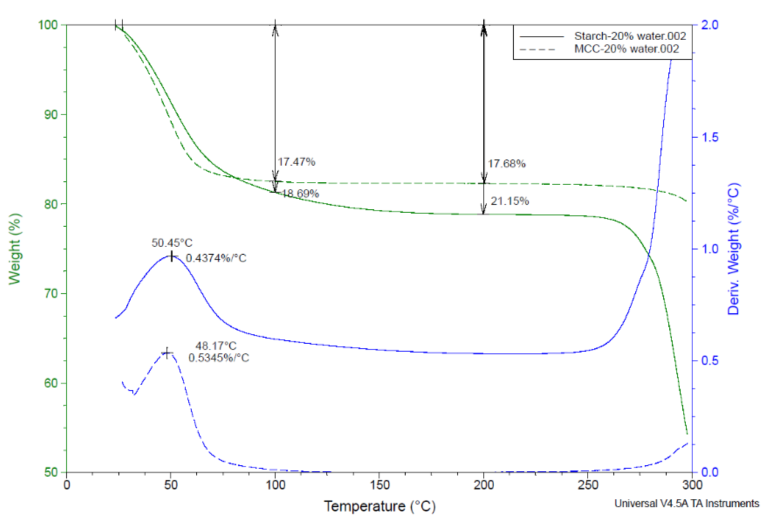


Figure 4: TGA Analysis of Starch 1500 and MCC Samples at 30% w/w Water Level

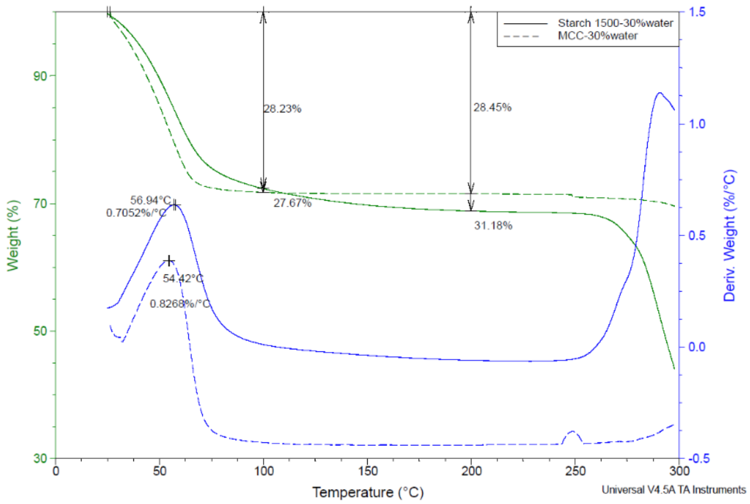


Table 1: Summary of TGA Analysis of Starch 1500 and MCC sample

Samples	Moisture Loss at 100°C (%)	Moisture Loss at 200°C (%)	Peak Moisture Evaporation Rate (%/°C)
Starch 1500 10% w/w water	11.1	14.2	0.29
MCC- 10% w/w water	10.4	10.5	0.21
Starch 1500- 20% w/w water	18.7	21.2	0.44
MCC- 20% w/w water	17.5	17.7	0.53
Starch 1500- 30% w/w water	27.7	31.2	0.71
MCC- 30% w/w water	28.2	28.5	0.83

Differential Scanning Calorimetry

Figures 4-6 show the results of DSC for heating and cooling cycles for MCC and Starch 1500 samples at 10, 20% and 30% w/w water. At 10% water level, Starch 1500 and MCC did not show a melting or freezing peak of water (Figure 5).

Figure 6 displays the DSC scan of 20% w/w samples where the heating cycles shows the water melting peak around 0°C from both samples; however, a significant difference in heat of melting MCC (17.0 J/g) and Starch 1500 (4.6 J/g) may suggest the absence of free water to melt in Starch 1500 sample. Consequently, MCC displayed a sharp water crystallization peak around -20°C in the cooling cycle while such a peak was absent for Starch 1500. Similar results were obtained for Starch 1500 and MCC containing 30% w/w water level (Figure 7). These results further indicate the presence of more bound water in Starch 1500 when compared to MCC.

Figure 4: DSC Analysis of Starch 1500 and MCC Samples at 10% w/w Water Level

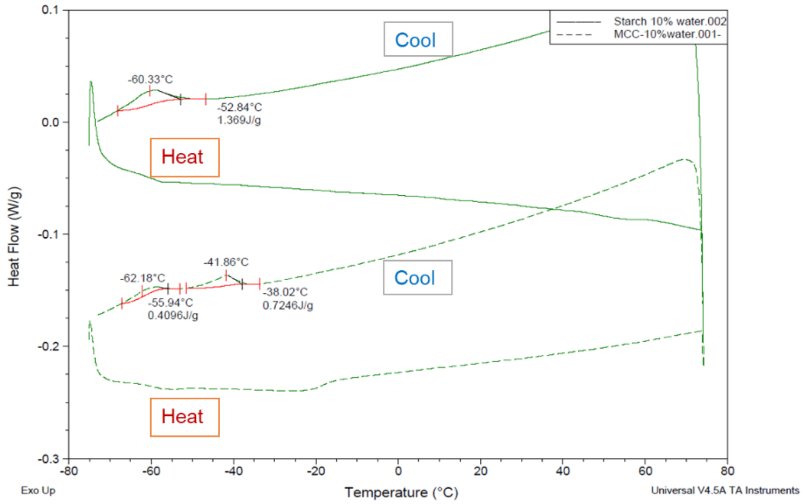


Figure 5: DSC Analysis of Starch 1500 and MCC Samples at 20% w/w Water Level

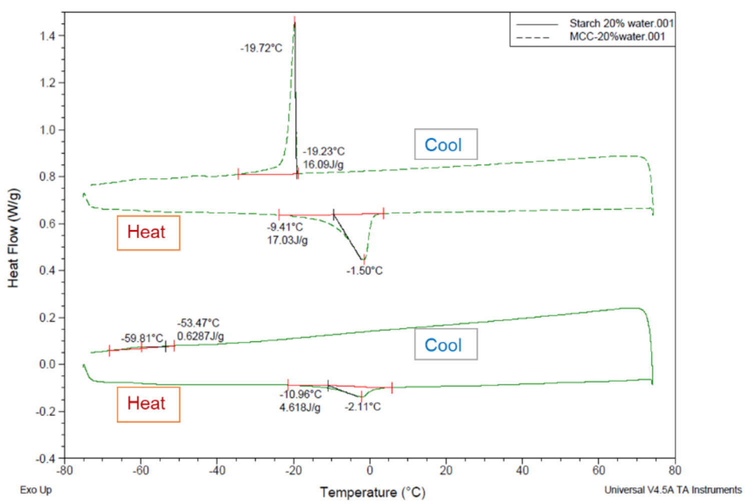
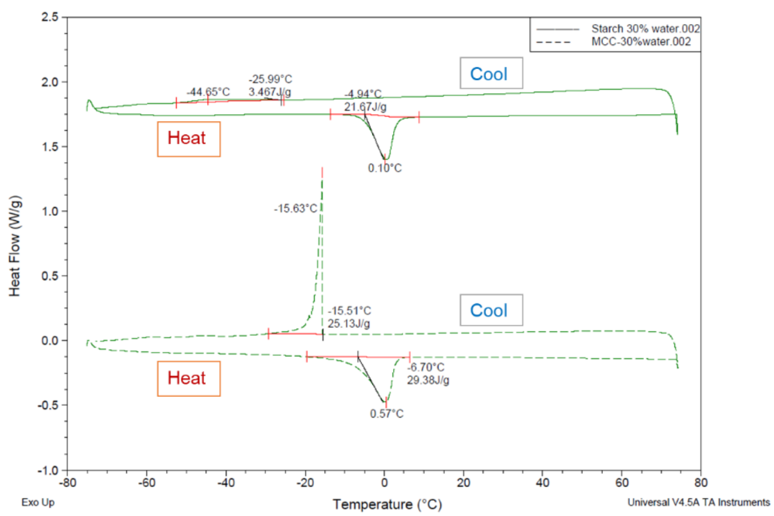


Figure 6: DSC Analysis of Starch 1500 and MCC Samples at 30% w/w Water Level



Conclusions

Moisture scavenging properties for two excipients, Starch 1500 and MCC, was analyzed using TGA and DSC analysis. TGA exhibited a slow dissociation of moisture, requiring more energy, from Starch 1500 indicating tightly bound water. DSC scans demonstrated an absence of sharp water crystallization peaks, with Starch 1500 samples indicating a lack of free water. The strong affinity of water for Starch 1500 may be utilized to scavenge free moisture in the microenvironment of a core formulation, which enhances the robustness of tablet and capsule formulations.

References

1. Cunningham CR, Kinsey B, Scattergood LK. Formulation of Acetylsalicylic Acid Tablets for Aqueous Enteric Film Coating. Pharmaceutical Technology, DRUG DELIVERY 2001, pp 38-43.