Impact of Temperature on Excipient Moisture Sorption Isotherms

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INTRODUCTION

- Moisture sorption isotherms (MSIs) are a critical item needed to determine drug product stability in packaging using stability modeling such as that implemented in the commercial software ASAP*prime*®
- Formulation isotherms have generally been assumed to be temperature-independent in the 25–40°C range relevant for stability programs, with MSIs typically taken only at 25°C
- This investigation was undertaken to determine if the assumption of temperature independence of MSIs is indeed accurate

EXPERIMENTAL METHODS

- MSIs for 16 common pharmaceutical excipients were measured using a dynamic vapor sorption (DVS) automated gravimetric system at 25 and 40°C
- Single sorption was measured at each temperature
- DVS was run with 10% RH steps (0–90% RH), equilibration method at dm/dt = 0.001%
- MSI data were fit to the Guggenheim-Anderson-de Boer (GAB) Equation in ASAP*prime*® (version 6.0.1):

$$Wt\%_{H_2O} = \frac{W_m CK(RH)}{[1 - K(RH)][1 - K(RH) + CK(RH)]}$$

- The excipient with the most pronounced difference between 25 and 40°C moisture sorption (povidone) was used to determine a worst-case differential in packaging, between assuming the 25°C sorption was the same at 40°C and using the actual 40°C sorption isotherm

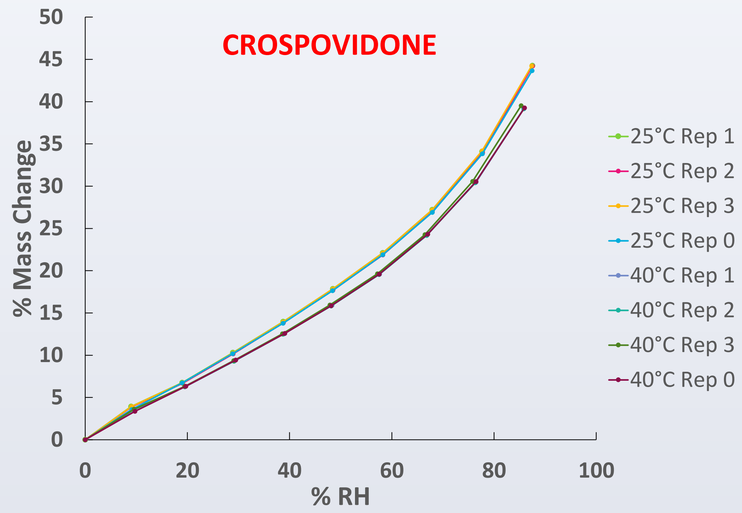
RESULTS

- Differences in MSIs measured at 25 and 40°C were observed for some excipients, no differences for others
- For excipients that do show difference, water uptake was typically reduced at 40 °C, consistent with entropic behavior

Waterman KC, Adami RC. Accelerated aging: prediction of chemical stability of pharmaceuticals. Int J Pharm. 2005;293:101-25.

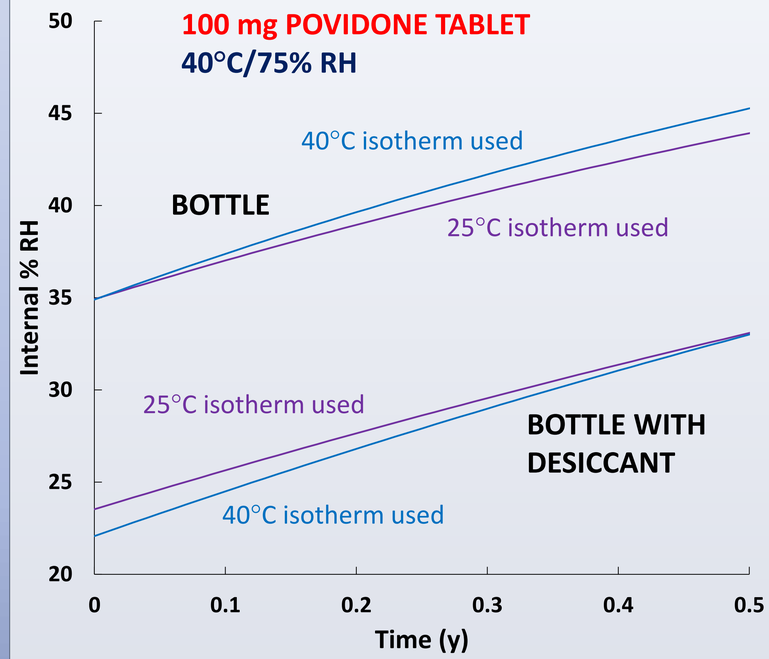
Maroulis, Z.B., E. Tsami, D. Marinos-Kouris, and G.D. Saravacos. "Application of the GAB Model to the Moisture Sorption Isotherms for Dried Fruits." *Journal of Food Engineering* 7, no. 1 (January 1988): 63–78.

ISOTHERM MEASUREMENTS



Excipient	% Water Uptake at 50% RH	
	25°C MSI	40°C MSI
Colloidal silicon dioxide	1.99	1.94
Copovidone	9.72	8.84
Croscarmellose sodium	12.59	11.82
Crospovidone	18.19	16.43
Hypromellose (E5)	4.86	4.47
Hypromellose (K100)	7.36	6.30
Kollicoat® IR	6.63	5.89
Kolliphor® P407	0.54	0.69
Lactose monohydrate	0.03	0.06
Magnesium stearate	0.87	0.86
Mannitol	0.08	0.12
MCC (Avicel® PH101)	5.54	5.09
MCC (Avicel® PH102)	5.36	5.04
Povidone	**18.48**	**15.76**
Pregalatinized starch	10.57	11.29
Sodium starch glycolate	12.98	12.96

MODEL RESULTS



60-cc HDPE (HIS) bottle, 30-count 100 mg povidone tablets, external conditions of 40°C/75% RH

CONCLUSIONS

- Temperature-dependent differences in MSIs are small
  - Even a pure tablet of the excipient having the greatest difference shows insignificant differences in the internal package RH as a function of time at 40°C/75% RH
- The assumption that MSIs generated at room temperature (25°C) are applicable to excipient behavior at increased temperatures (40°C) is shown to be valid

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