



## THERMAL STABILITY OF API'S UNDER HIGH TEMPERATURE HPLC CONDITIONS

### INTRODUCTION

Temperature programmed HPLC at elevated temperatures can replace solvent gradients and simplify method development. Many analysts, particularly in the pharmaceutical industry, have concerns about the thermal stability of their compounds. This technical note evaluates several active pharmaceutical ingredients (API's) at elevated temperatures and looks for evidence of thermal degradation.

### EXPERIMENTAL

Three compounds, Dexamethasone, Carbamazepine, and Lansoprazole were selected for evaluation. All three were commercially available and had recommended storage temperatures from 2°C to 8°C for the API. Solutions of each compound were prepared and analyzed by HPLC at temperatures between 40°C and 100°C in ten degree increments.

HPLC conditions are summarized in Table 1. The HPLC system consisted of an Alltech vacuum degasser, Knauer pump and UV detector, an Alcott autosampler, and a Polaratherm Series 9000 Total Temperature Controller.

### RESULTS

Table 2 and Figure 1 has results for the analysis of Dexamethasone. Table 2 shows peak areas at temperatures from 40 to 100°C and Figure 1 shows the actual chromatograms. Table 3 and Figure 2 show the same data for Carbamazepine, and Table 4 and Figure 3 contain the data for Lansoprazole.

The Dexamethasone and Carbamazepine showed no loss of peak area, baseline rise, or poor peak shape with increasing temperature. Poor peak shape, extra peaks, and a loss of peak area would indicate evidence of thermal decomposition. The Lansoprazole showed a rise in the baseline and a loss of peak area at 70°C. This becomes more pronounced at 80°C. By 100°C, over half of the Lansoprazole had decomposed (determined by peak area).

### CONCLUSIONS

Although Lansoprazole did show some thermal decomposition, the Dexamethasone and Carbamazepine appeared to be thermally stable to 100°C. Many pharmaceuticals can probably be analyzed at elevated temperatures without concerns about thermal degradation, but some analytes will thermally decompose. Please refer to Tech note 801 for additional information on thermal stability of analytes.

Table 1 Conditions for Analysis of API's for Thermal Stability	
Column:	Selerity Blaze C <sub>8</sub> 100 x 4.6 mm, 3 um
Mobile Phase:	50:50 Acetonitrile:Water
Flow:	1.0 mL/min
Detection:	UV @ 254 nm
Injection:	5 uL
Temperature:	40, 50, 60, 70, 80, 90 and 100°C



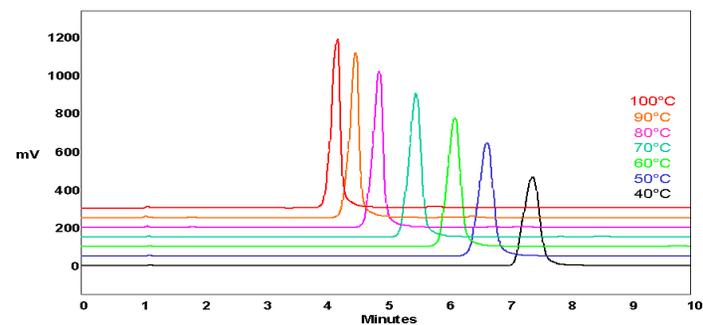
Table 2. Peak area vs temperature for the HPLC analysis of Dexamethasone

Figure 1. Chromatograms showing the HPLC analysis of Dexamethasone at temperatures from 40 to 100°C

### Analysis of Dexamethasone

Temperature	Peak Area
40°C	9,997,556
50°C	10,387,062
60°C	10,777,056
70°C	9,991,160
80°C	9,609,552
90°C	9,911,457
100°C	9,745,998
<b>Mean</b>	<b>9,987,856</b>
<b>%RSD</b>	<b>6.97%</b>

### Analysis of Dexamethasone



### Analysis of Carbamazepine

Temperature	Peak Area
40°C	10,122,934
50°C	10,078,074
60°C	9,941,243
70°C	9,785,801
80°C	9,749,546
90°C	9,348,786
100°C	9,835,455
<b>Mean</b>	<b>9,837,405</b>
<b>%RSD</b>	<b>2.99%</b>

### Analysis of Carbamazepine

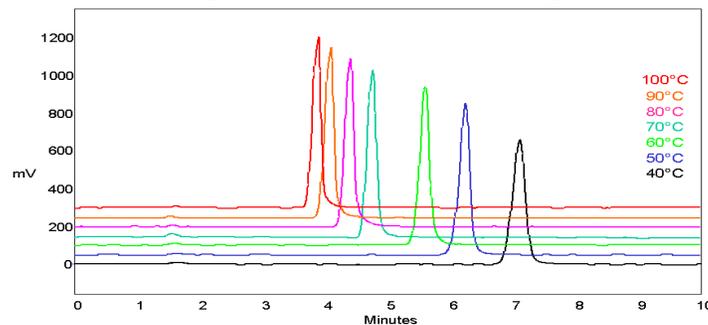


Table 3. Peak area vs temperature for the HPLC analysis of Carbamazepine

Figure 2. Chromatograms showing the HPLC analysis of Carbamazepine at temperatures from 40 to 100°C

Table 4. Peak area vs temperature for the HPLC analysis of Lansoprazole.

Figure 3. Chromatograms showing the HPLC analysis of Lansoprazole at temperatures from 40 to 100°C

### Analysis of Lansoprazole

Temperature	Peak Area
40°C	10,507,929
50°C	10,194,359
60°C	9,851,429
70°C	9,070,418
80°C	7,513,678
90°C	5,977,033
100°C	4,082,027

### Analysis of Lansoprazole

