A method was developed and validated to quantify the drug metabolite terfenadine in human serum and plasma across the range of 5 ng/mL to 200 ug/mL. Calibrators were broken into two separate regions, with partial overlap, to accommodate the broad range necessary. Matrix effects were evaluated carefully in several collection tube types and with special matrix types of lipemic, icteric, and hemolysed conditions.

The majority of patient samples fall in the range of the upper calibration curve (above). If a sample falls below the LOD of the upper curve then the lower calibration curve is used.

The method uses simple protein precipitation. Supernatant from the upper curve analysis is diluted 100x before injection while lower curve injection is without dilution.

Separation is performed on a pentafluorophenyl phase.

**RESULTS**

**EXTRAPOLATION VS SPLIT CURVE RANGE**

Analytical Measurement Range by Extrapolation

A linear fit is extrapolated beyond the range of the calibrators and up to some higher desired concentration. Quantitative accuracy across the entire concentration range is verified every 6 months.

**MATRIX AND TUBE TYPE EFFECTS**

<table>
<thead>
<tr>
<th>Std 2</th>
<th>Cond</th>
<th>Std 8</th>
<th>Cond</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Mean</td>
<td>Mean</td>
<td>Serum</td>
</tr>
<tr>
<td>0.00519</td>
<td>0.00497</td>
<td>98.2%</td>
<td>0.00497</td>
</tr>
<tr>
<td>Water ctrl.</td>
<td>0.00525</td>
<td>Water ctrl.</td>
<td>0.00507</td>
</tr>
<tr>
<td>0.00519</td>
<td>0.00497</td>
<td>98.2%</td>
<td>0.00497</td>
</tr>
</tbody>
</table>

**COLLECTION TUBE EXPERIMENTS**

An original run time with lengthier column washing produced the results below and in tables at right. Shortening the injection cycle to 4 minutes yielded a broadened, slightly early eluting peak, with gray topped (NaF/K Oxalate) tubes (below right).

**CONCLUSIONS**

- An accurate and precise method has been developed and validated for terfenadine.
- A very broad quantitative range is accommodated by splitting the concentration curve into two overlapping segments.
- The importance of conducting thorough anti-coagulant and matrix effect studies is emphasized.
- Qualitatively, lipemic, icteric, and hemolysed samples do not appear to produce significantly increased ionization suppression compared with a control matrix.

**ACKNOWLEDGEMENTS**

Thanks are given to the ARUP Institute for Clinical and Experimental Pathology for making this work possible.