

---

# Ultrahigh-Pressure LC (UHPLC): Benefits and Issues in Pharmaceutical Analysis

Michael W. Dong  
Sr. Scientist, Small Molecule Analytical Chemistry and QC  
Genentech

*Interview in the LCGC and Spectroscopy 2011 Pittcon Theater  
(Atlanta, Georgia, March 14 & 15, 2011)*

# 1. UHPLC: a Modern Platform!

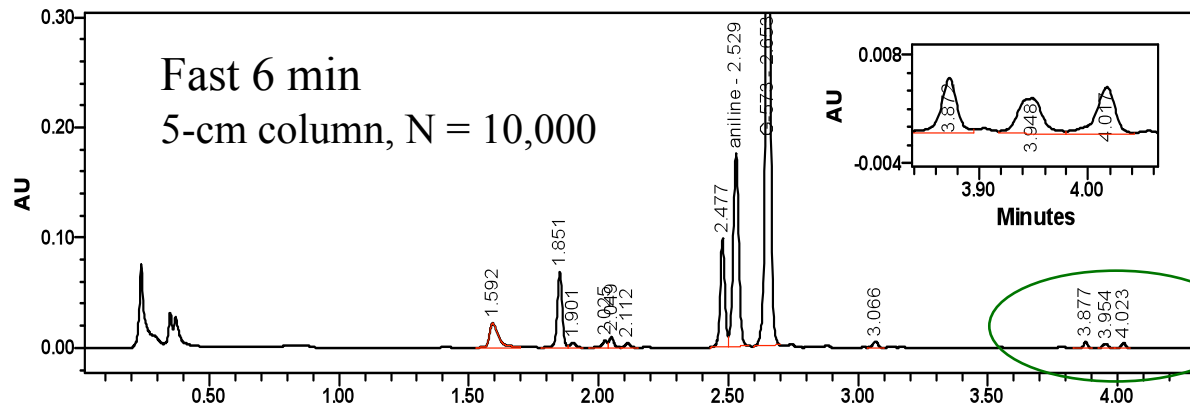
15,000 – 19,000 psi

1. Waters Acquity UPLC<sup>®</sup> (2004)-**15,000 psi**
  - UPLC H-Class\* and Bio\* (2010)
2. Jasco Extreme LC (2004) -**15,000 psi**
3. Thermo Accela\* (2006) -**15,000 psi**
  - Accela 1250\* (**19,000 psi**, 2010)
4. Dionex Ultimate 3000\* (2008) -**12,000 psi**
  - (**15,000 psi**, 2010)
5. Perkin Elmer Flexar\* (2009) -**18,000 psi**
6. Agilent 1290 Infinity (2010) – **18,000 psi**
  - 1260\* (9,000 psi, 2010)
7. Shimadzu Nexera (2010) – **19,000 psi**

•Quad pump available



## 2. Benefits: High-speed or ultra-high-resolution mode

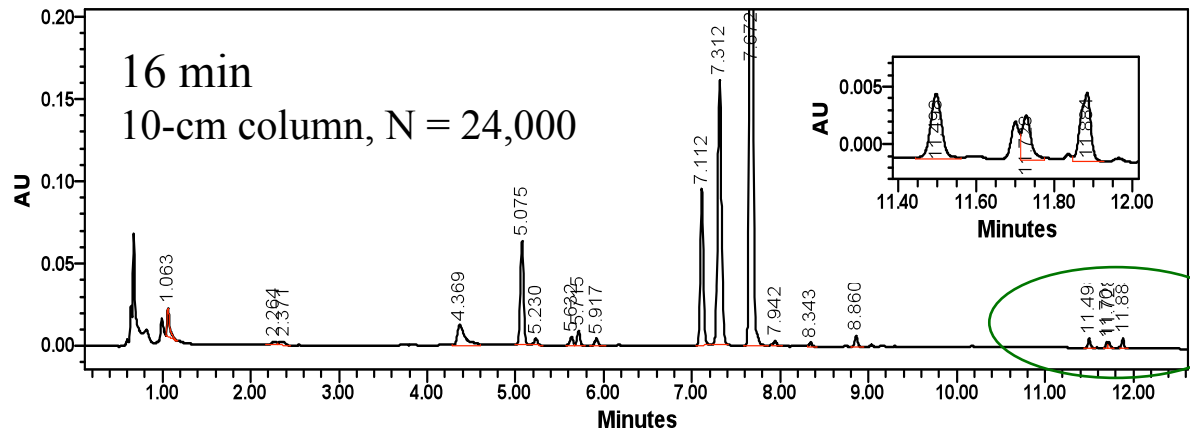


Column: RP polar-embedded  
(1.7  $\mu$ m, 50 x 2.1mm)

Mobile Ph.: A1: 0.05% formic acid  
B1: ACN

Solvent prog: 20% B to 60% in 3 min

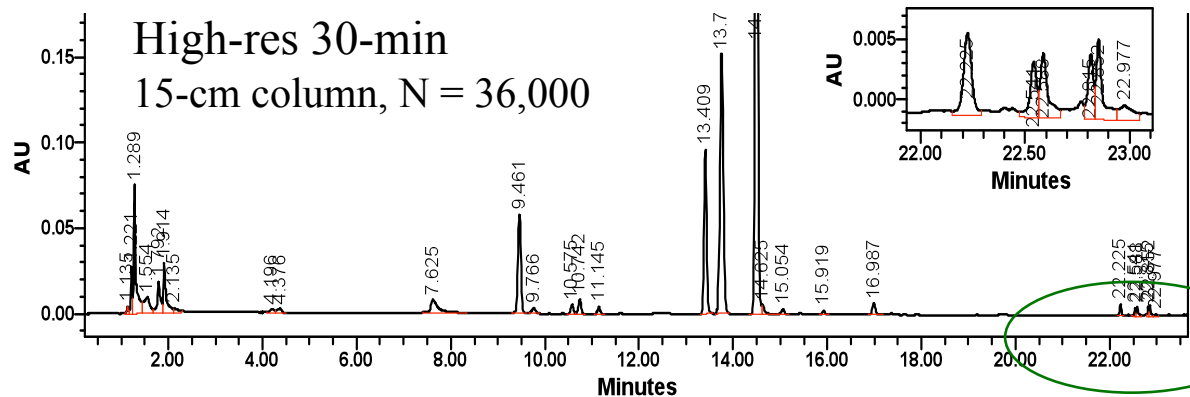
Flow Rate: 0.6 mL/min @ 30C 9000 psi



Solvent prog: 20% B to 60% in 10 min

Flow Rate: 0.4 mL/min @ 30C 8000 psi

***Benefit: very high resolution.  
in reasonable time.***



Solvent prog: 20% B to 60% in 20 min

Flow Rate: 0.3 mL/min @ 30C 11000 psi

## 3. Potential Issues

---

1. Safety issues
2. Viscous heating
3. System and operating nuances
  - Equipment cost, operating training
  - System dispersion, dwell volumes
  - Compatibility to conventional columns and existing methods
  - Column availability, life time
4. Injection precision
5. Detector sensitivity
  - Pump blending of UV absorbing MP with detection at low  $\lambda$
6. Method portability

## 4. Alternatives to UHPLC

---

1. Sub-3-  $\mu$ m columns
  - Sub-3-  $\mu$ m should be more compatible to conventional HPLC
2. Monoliths
3. Fuse Core columns
4. High-temperature LC
5. Multi-parallel LC

## 5. Myths

---

- “We designed our UHPLC to match sub-2  $\mu$ m columns”
- “We have the lowest dwell volumes!”
  - Binary high-pressure mixing pump is a “must”
- “Viscous heating is real problem”
  - Sub-2  $\mu$ m columns must be 2 mm i.d. or smaller
- “Method transfer is a piece of cake”
  - Method re-validation is not needed
- “We use gold plated fittings with double ferrules”

# Summary:

## Potential UHPLC Issues

---

- Safety issues ✓ ✓ ✓
  - Viscous heating ✓ ✓ ✓
  - System and operating nuances
    - Cost, training, dispersion, dwell volumes ✓ ✓
    - Compatibility to conventional columns and existing methods ✓ ✓ ✓
    - Column availability, life time ✓ ✓ ✓
  - Injection precision and carryover ✓ ✓ ✓
  - Detector sensitivity (pump blending problems) ✓ ✓ ✓
  - Method portability ✓ ✓ ✓
- Reassessed in Feb 2011

*UHPLC is going mainstream and is ready for pharm analysis!*