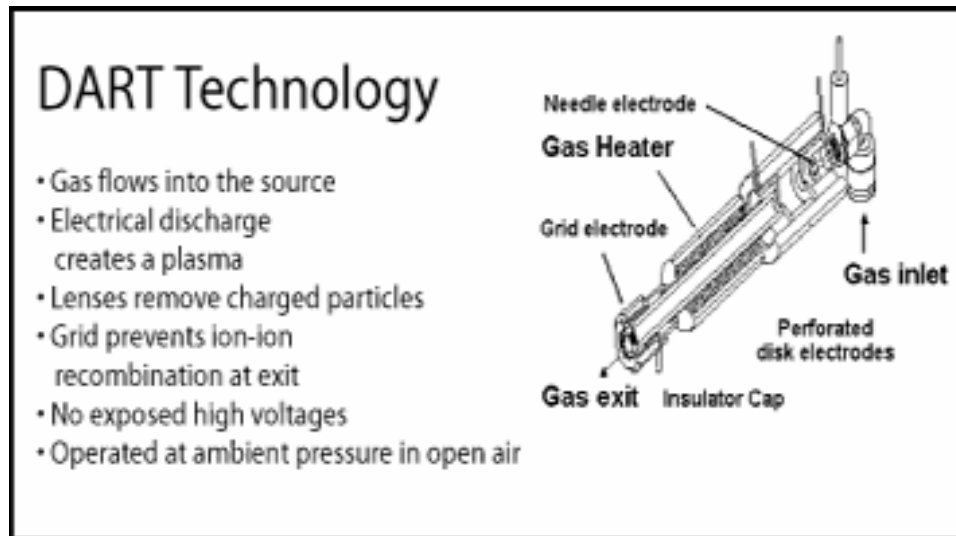


# Strategies for Rapid Determination of Impurities using DART-MS from Surfaces

Brian Musselman, Elizabeth  
Crawford, Catherine Stacy and  
Robert Cody

IonSense, Inc.  
Saugus, MA,. USA

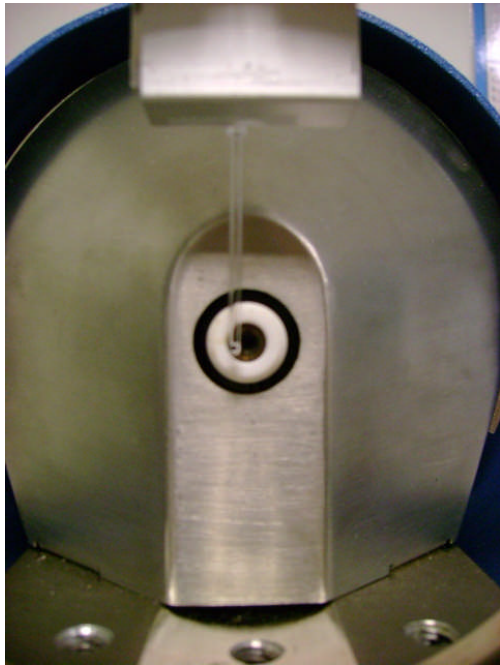
# DART Ionization Source



- Instantaneous ionization of solids, liquids, gases
- Little sample preparation
- Mass range up to 2000 Da
- Interfaced to a various commercial LC/MS

# Typical DART Sampling

Position a liquid or solid in path of carrier gas



# Representative Sample

## Well Characterized OTC Product



# Tylenol Cold Caplets

- **Day Caplet**

- Acetaminophen
  - 325 mg/caplet
- Dextromethorphan HBr
  - 10 mg/caplet
- Phenylephrine HCl
  - 5 mg/caplet

- **Night Caplet**

- Acetaminophen
  - 325 mg/caplet
- Dextromethorphan HBr
  - 10 mg/caplet
- Phenylephrine HCl
  - 5 mg/caplet
- **Chlorpheniramine Maleate**
  - **2 mg/caplet**

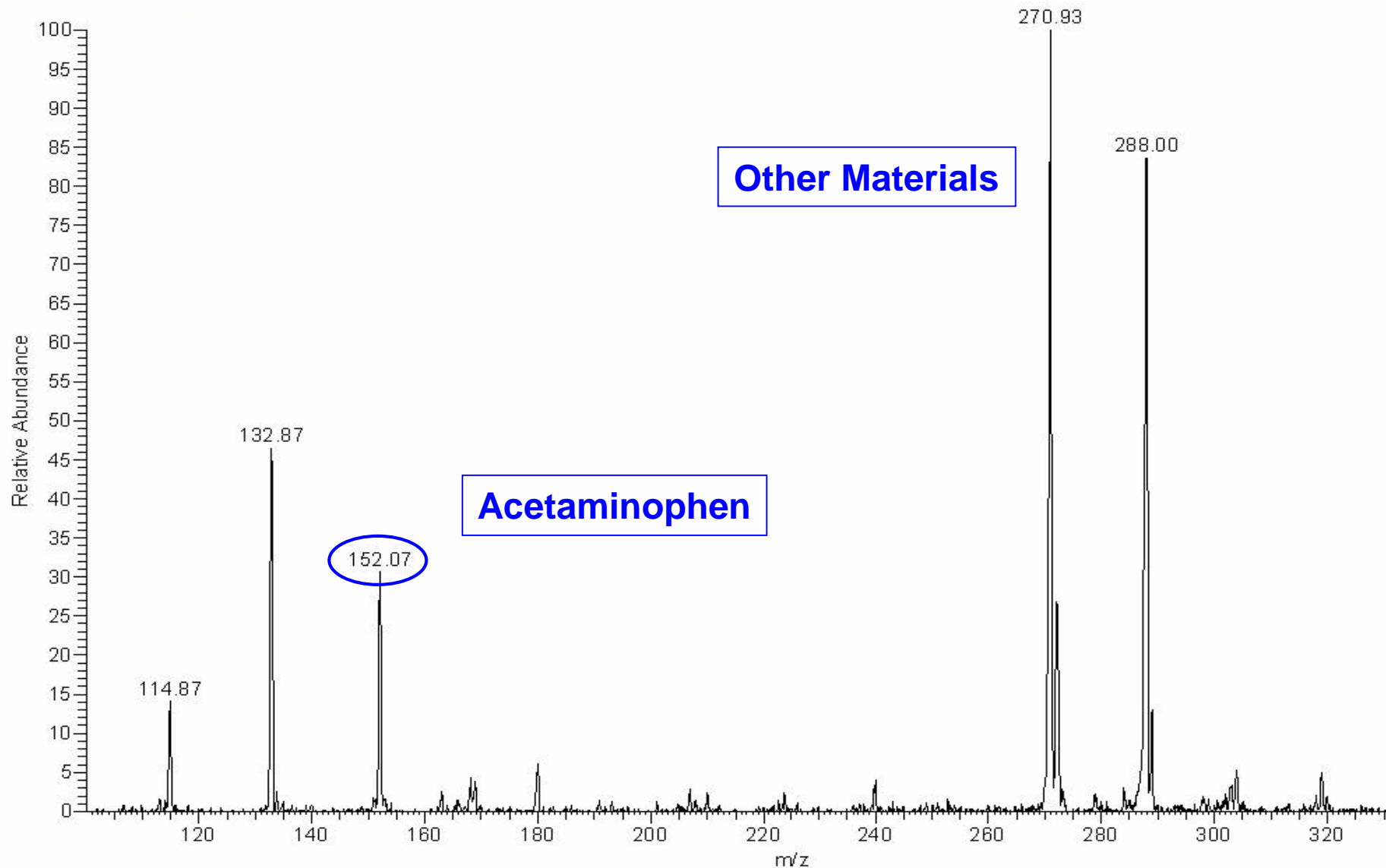
# Method Development

Position Sample in Holder  
Vary Desorption Temperature  
Vary Speed of Sampling

DART-ET on the LCQ  
DART-ET set at 15 ° Angle

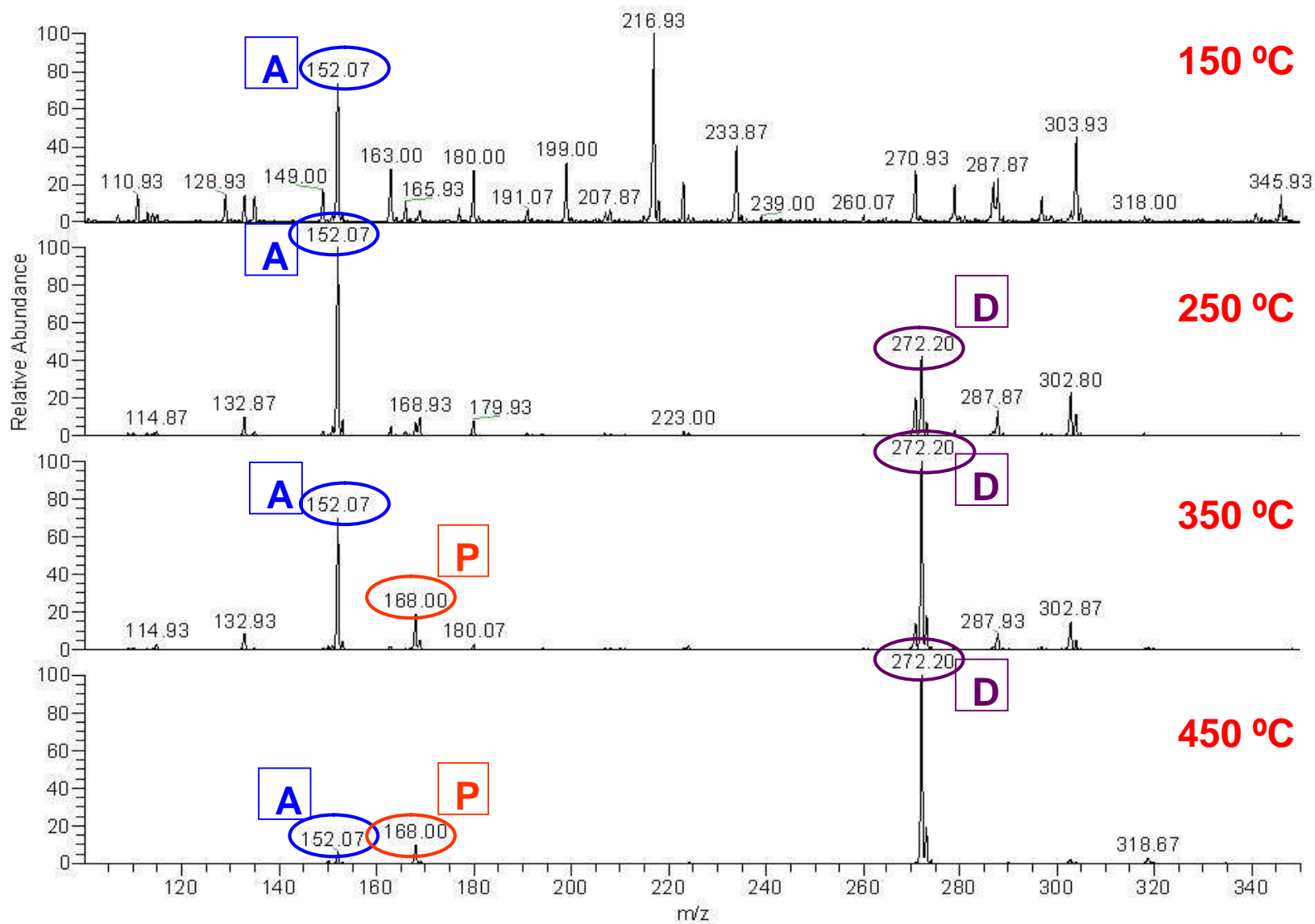


# Without a Strategy Caplet Analysis DART-ET 250 °C

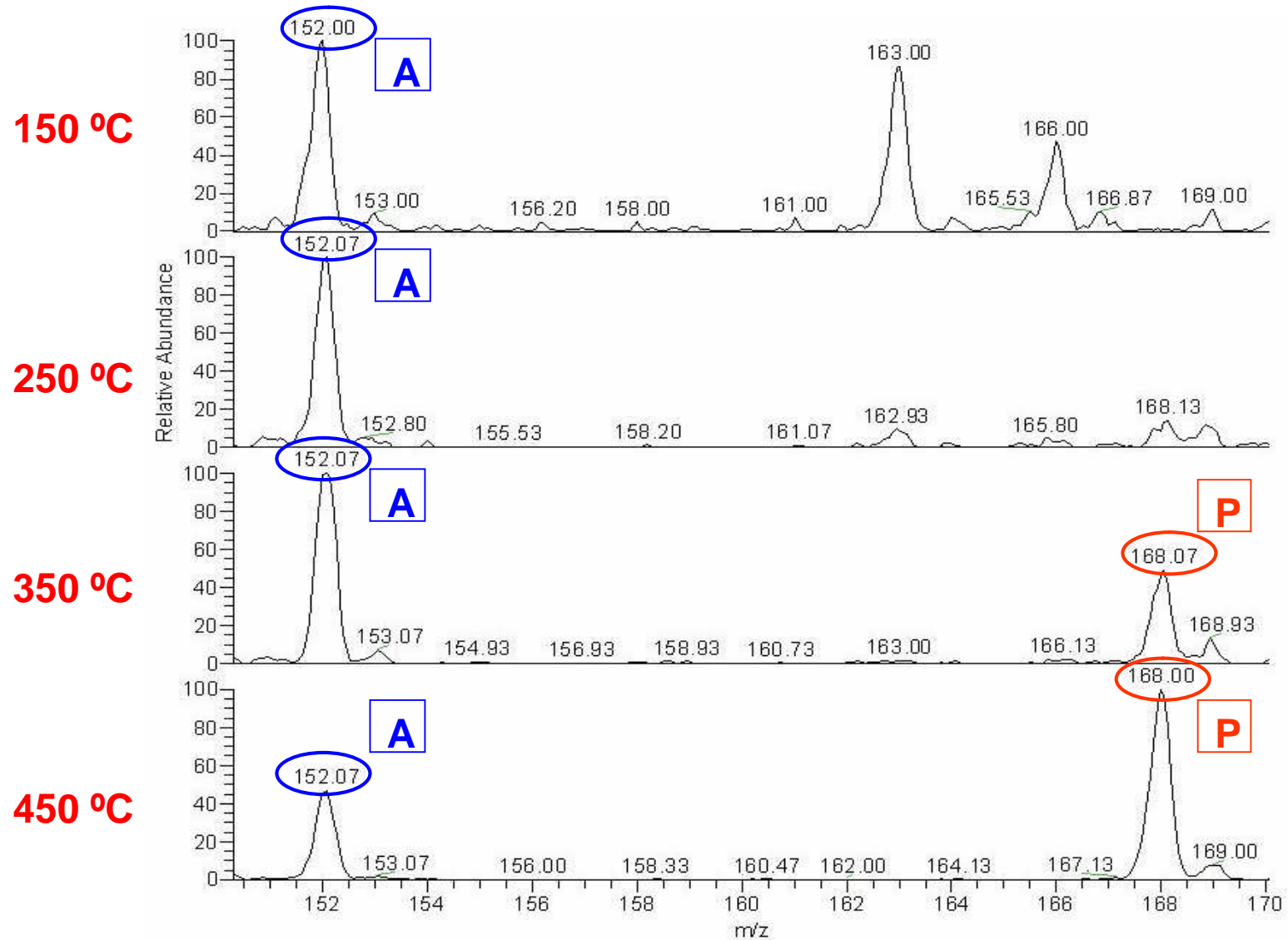


# Temperature Profile Phase of Method Development

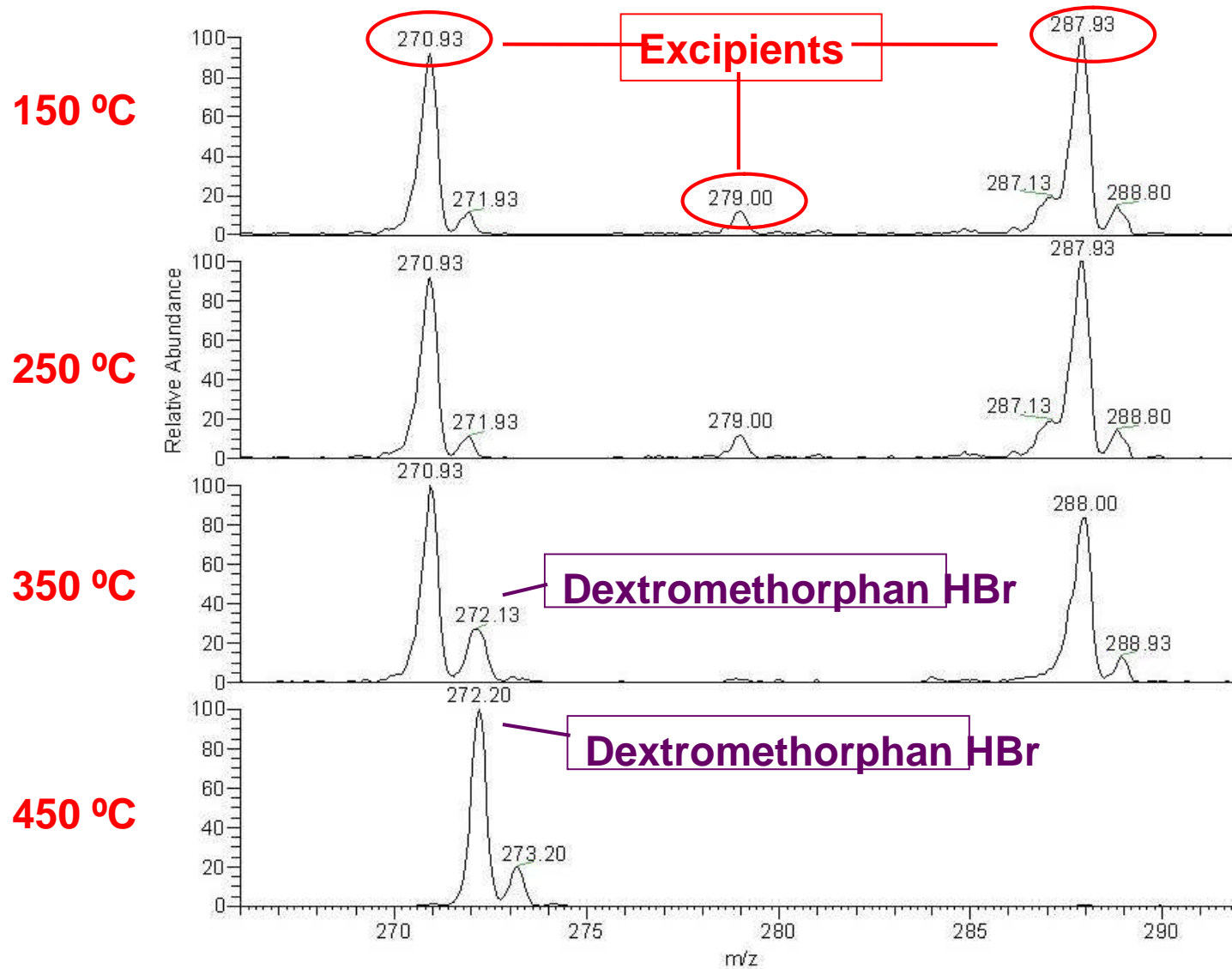
## Daytime Caplet – 4 DART-ET Temperatures - Search for 3 Active Ingredients



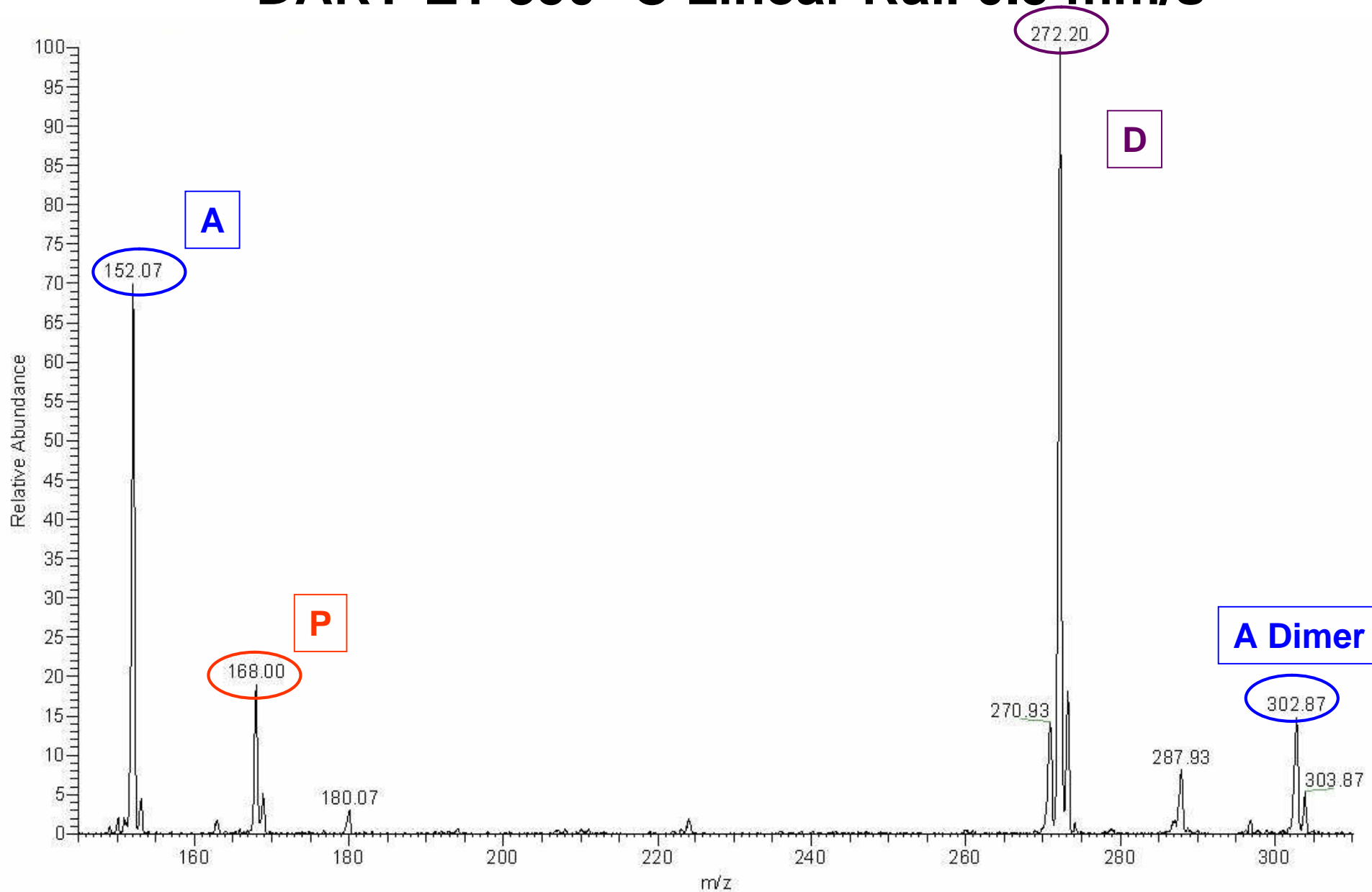
# Mass Chromatogram for Protonated Active Ingredients



# Mass Chromatogram for Protonated Active Ingredients



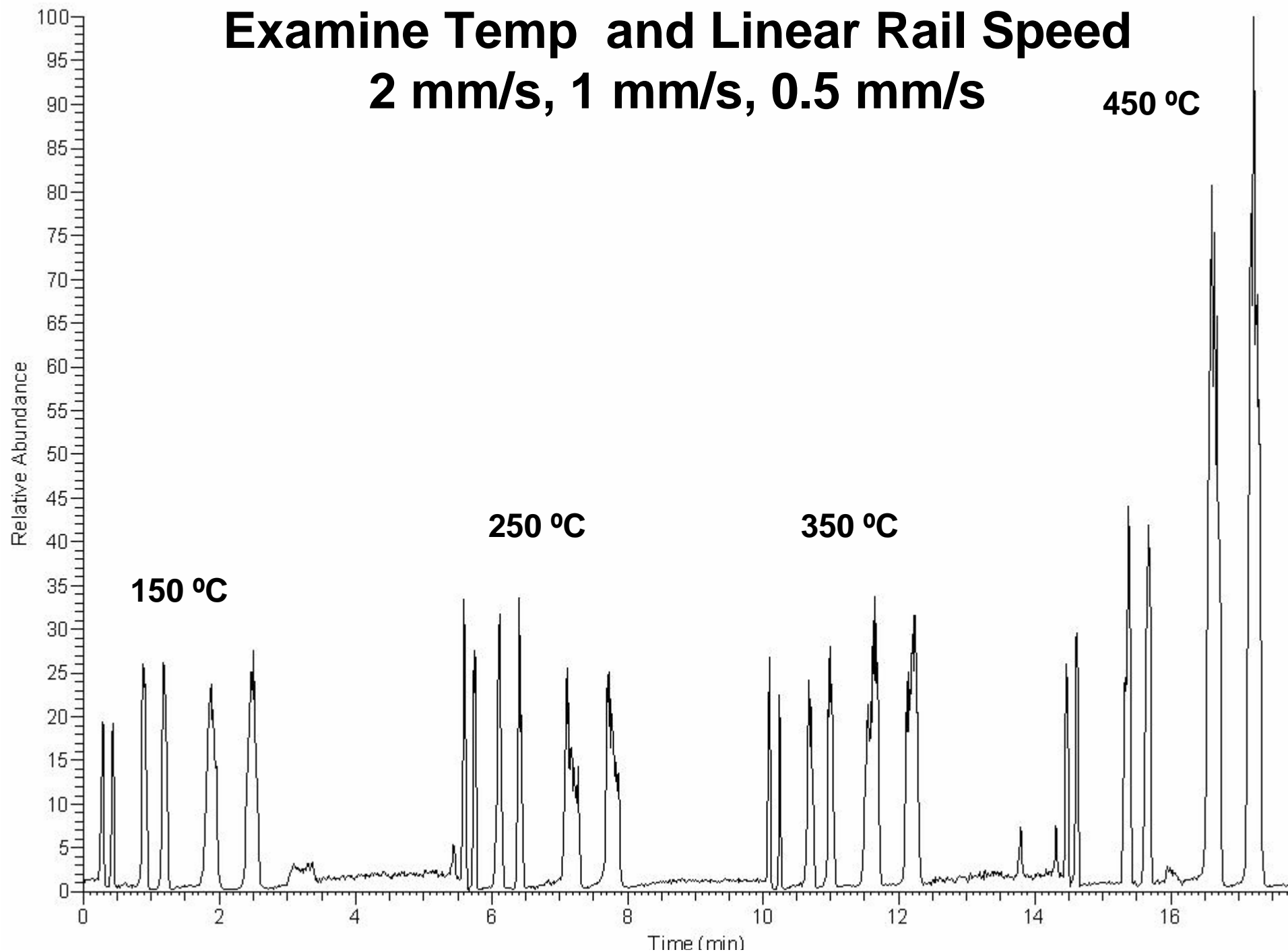
# DART-ET 350 °C Linear Rail 0.5 mm/s



# Examine Temp and Linear Rail Speed

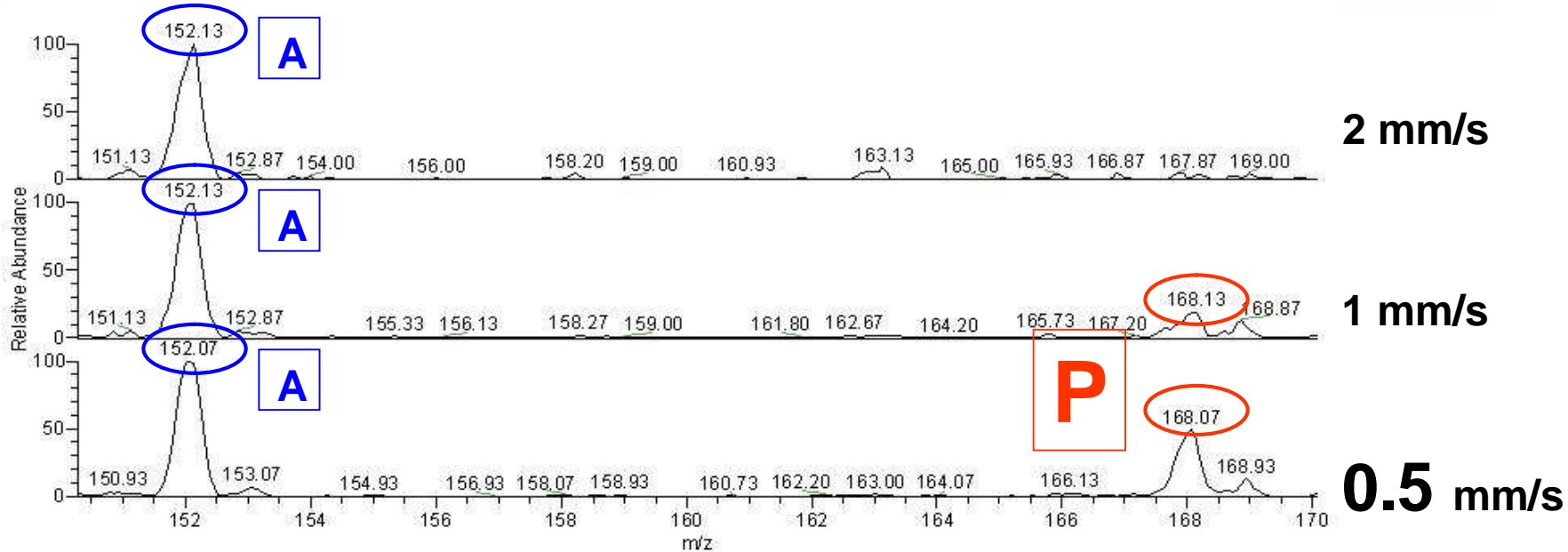
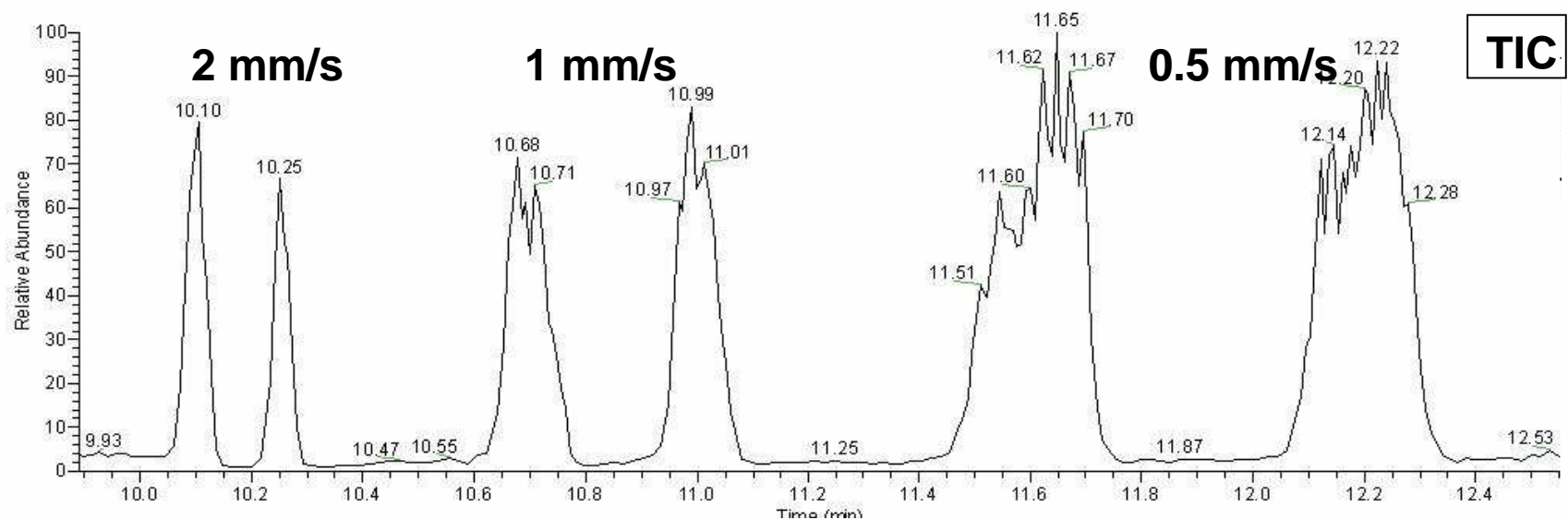
2 mm/s, 1 mm/s, 0.5 mm/s

450 °C



# Daytime Caplet DART-ET 350 °C

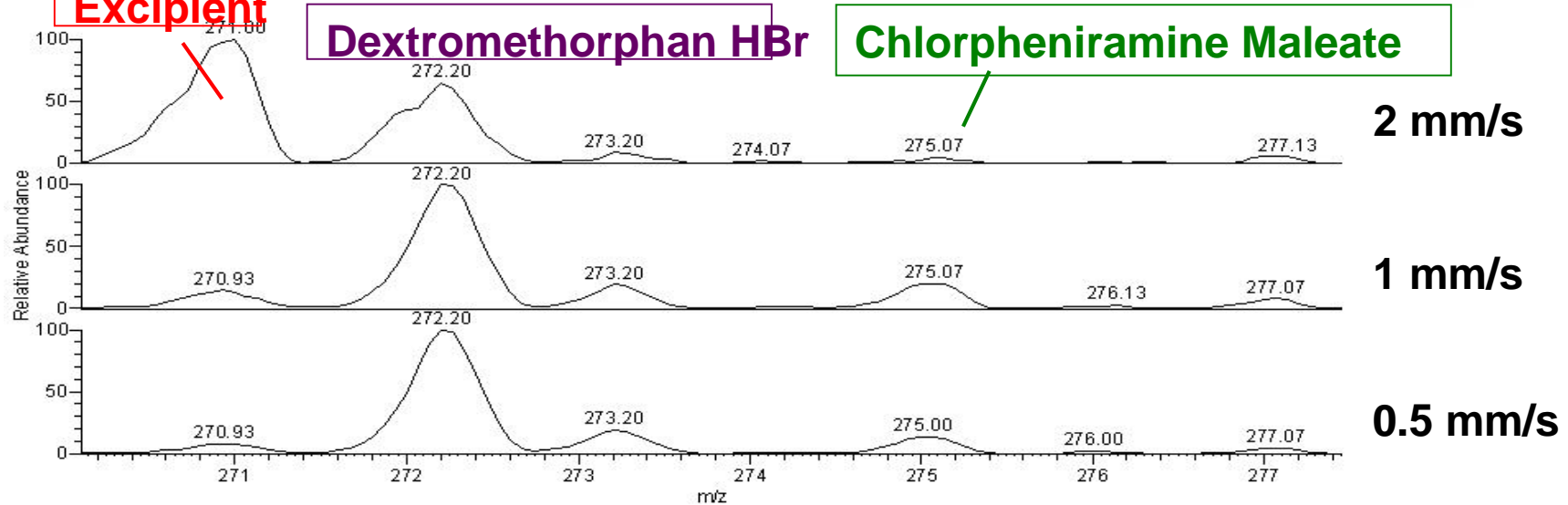
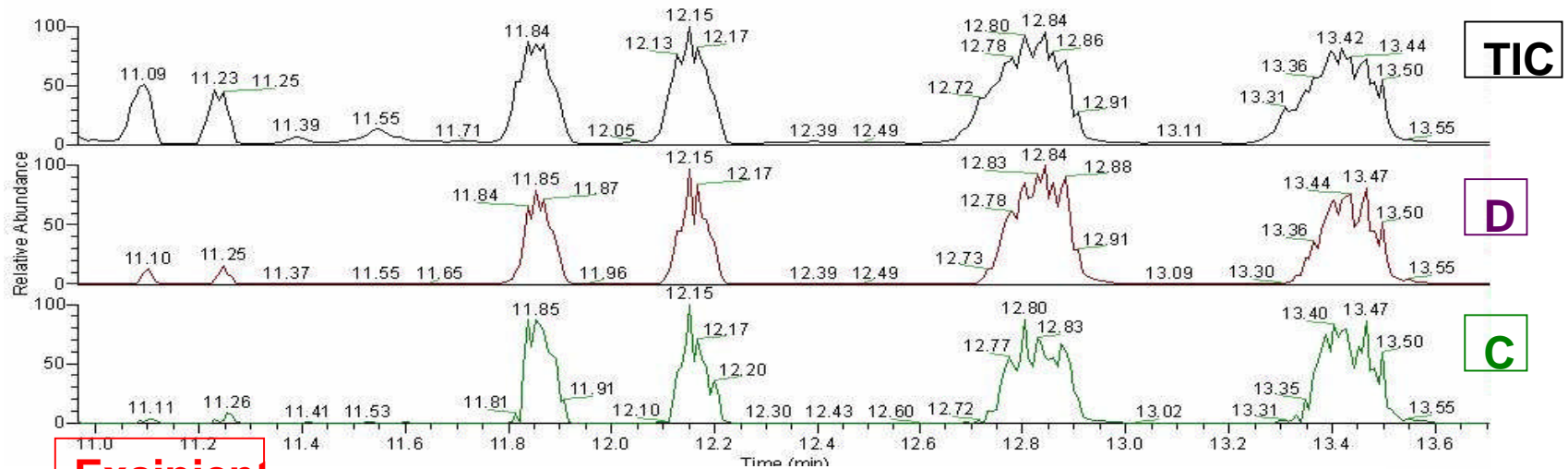
0.5 mm/s yields more diverse representation of product



# Treat the Nighttime Caplet Test Case

## Use the Method DART-ET 350 °C

### Varv Linear Rail Speeds

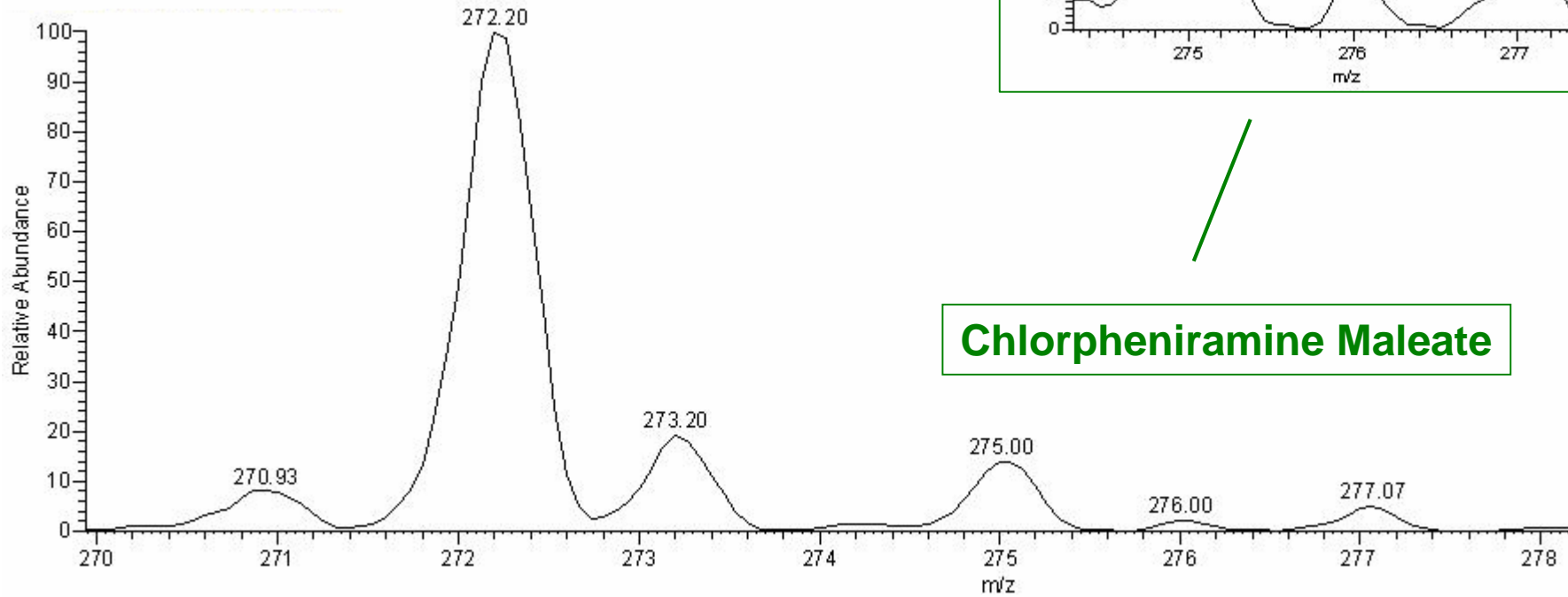


# Nighttime Caplet

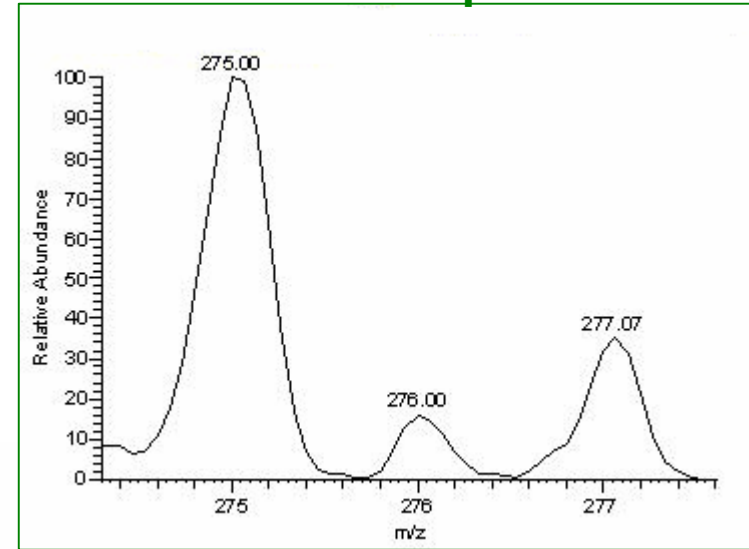
DART-ET 350 °C

Linear Rail Speed 0.5 mm/s

Dextromethorphan HBr



## 1 Chlorine Isotope Pattern



Chlorpheniramine Maleate

Not Everything is a Caplet

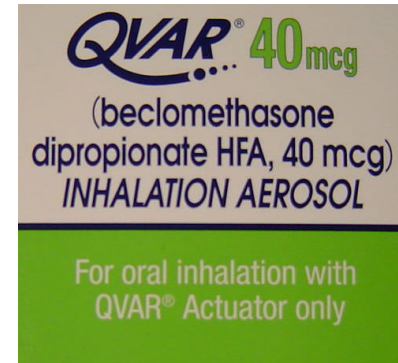
# Inhalers

Experiments with the DART-ET on the LCQ

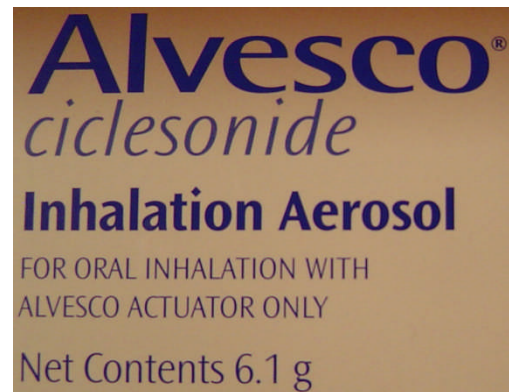
DART-ET set at 45 ° Angle

# Aerosol Inhalers on Filter Paper

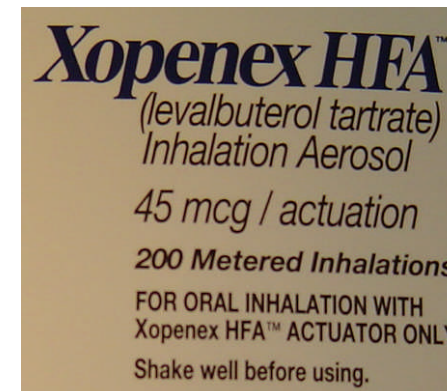
- Qvar (40 mcg)
  - Beclomethasone dipropionate HFA



- Alvesco (80 mcg)
  - Ciclesonide

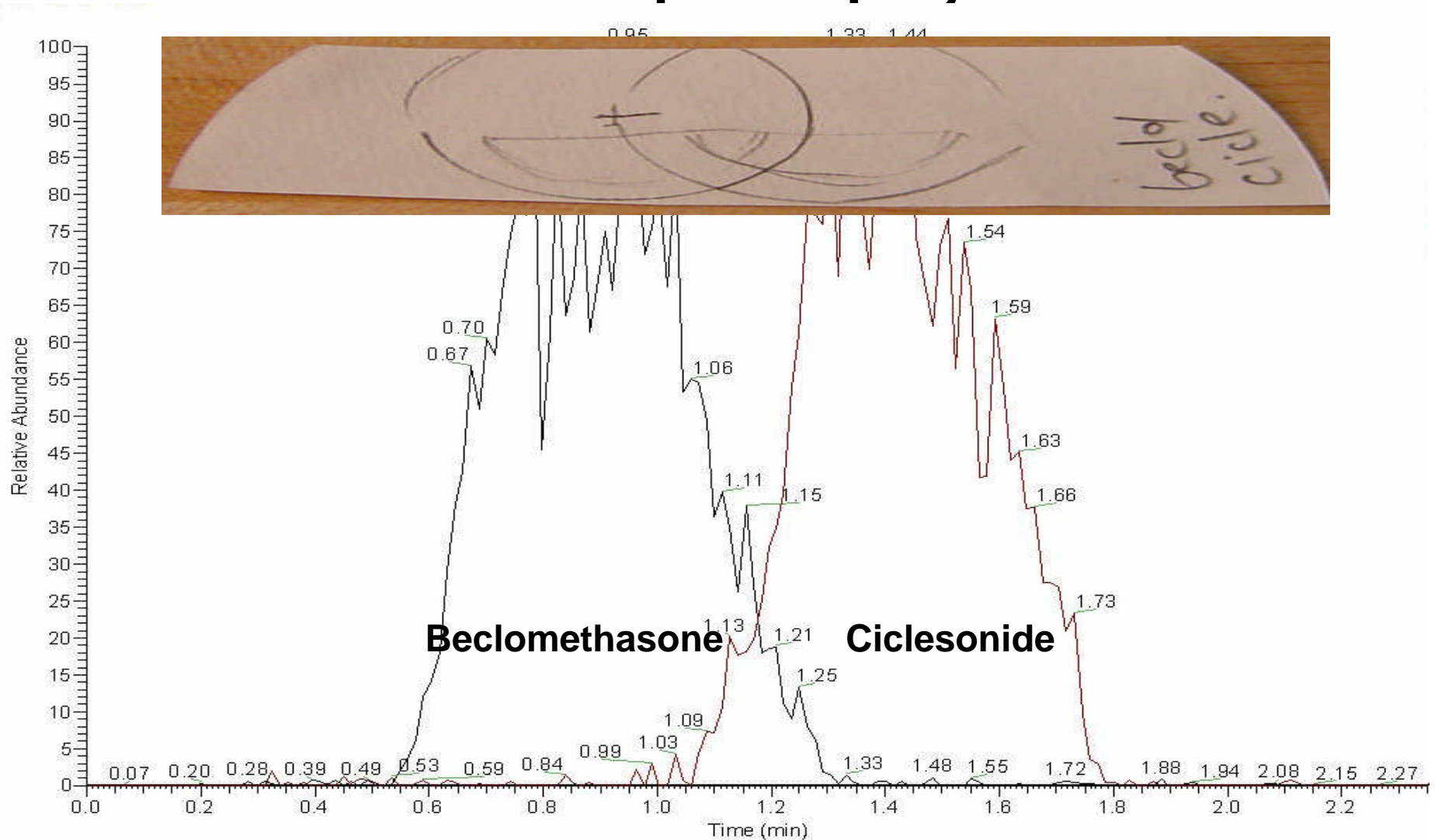


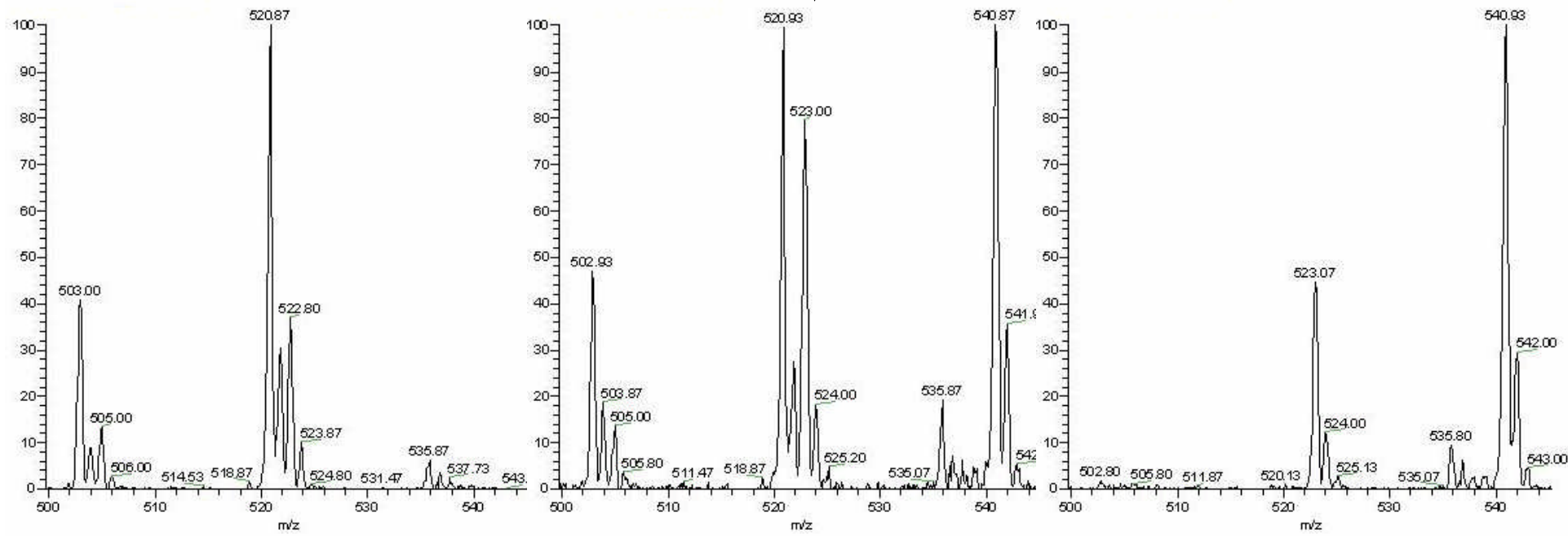
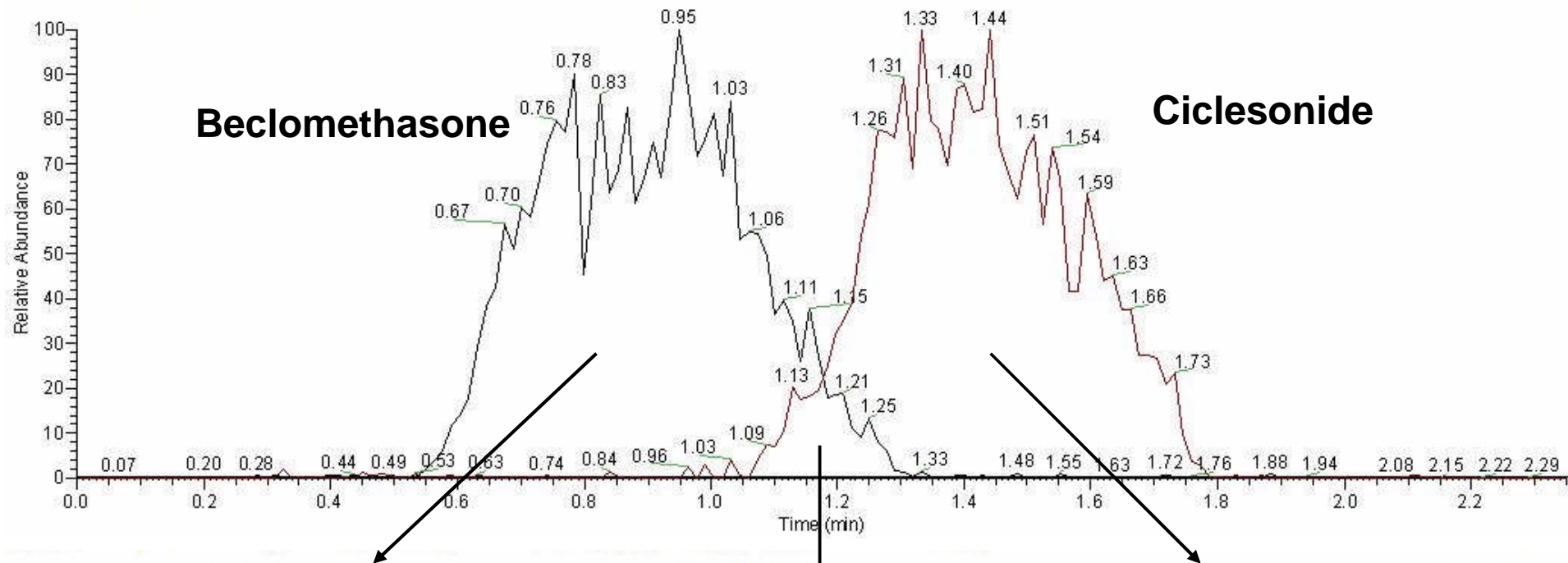
- Xopenex HFA (45 mcg)
  - Levalbuterol tartrate



# Spray Different Inhalers onto Filter Paper

## Overlap the Spray

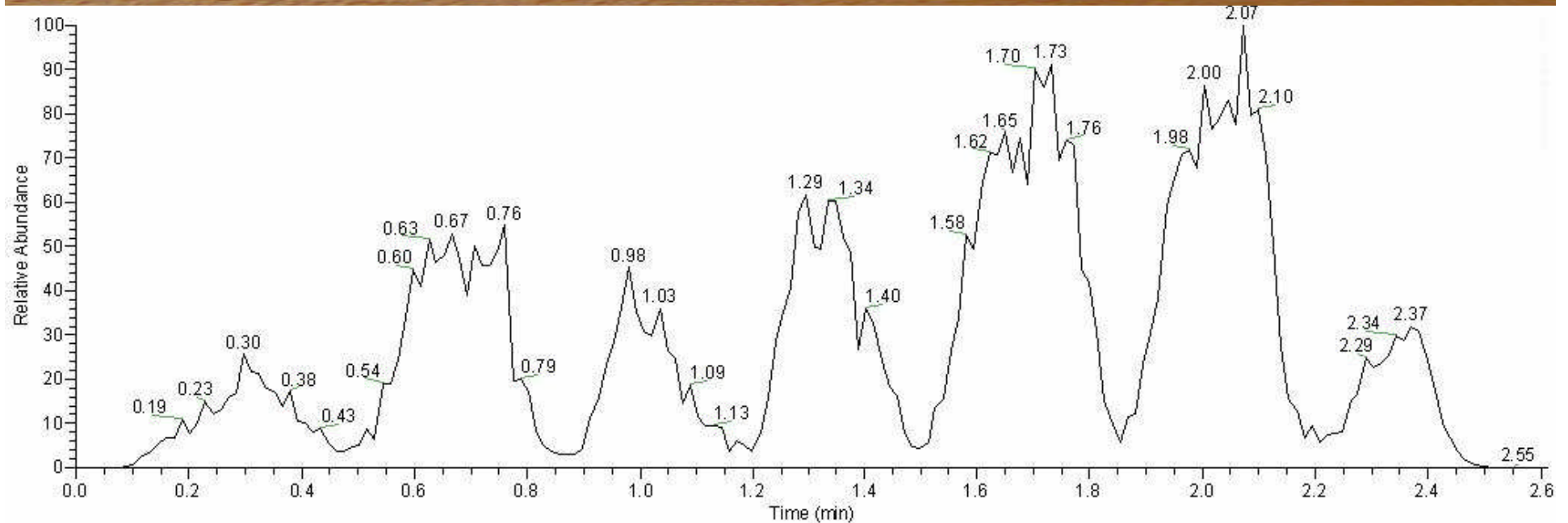
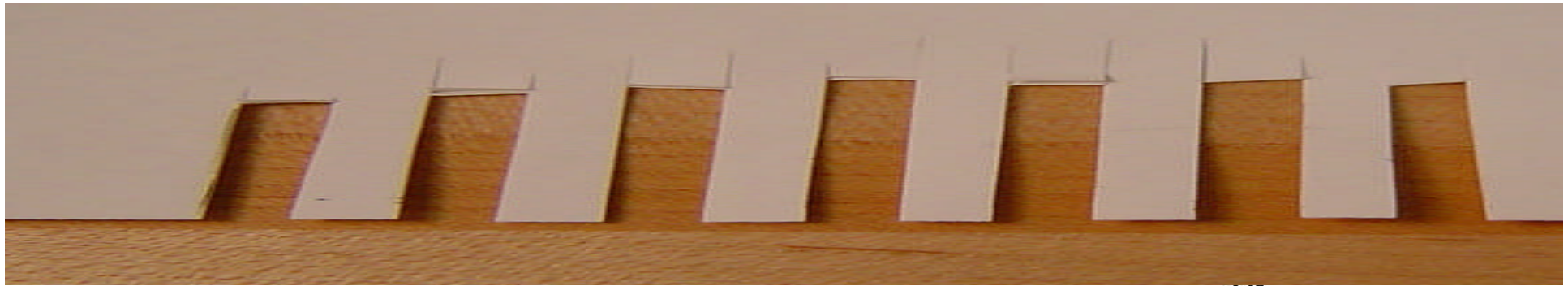




# How Fast? - 7 / 2 minutes

Xopenex HFA Inhaler

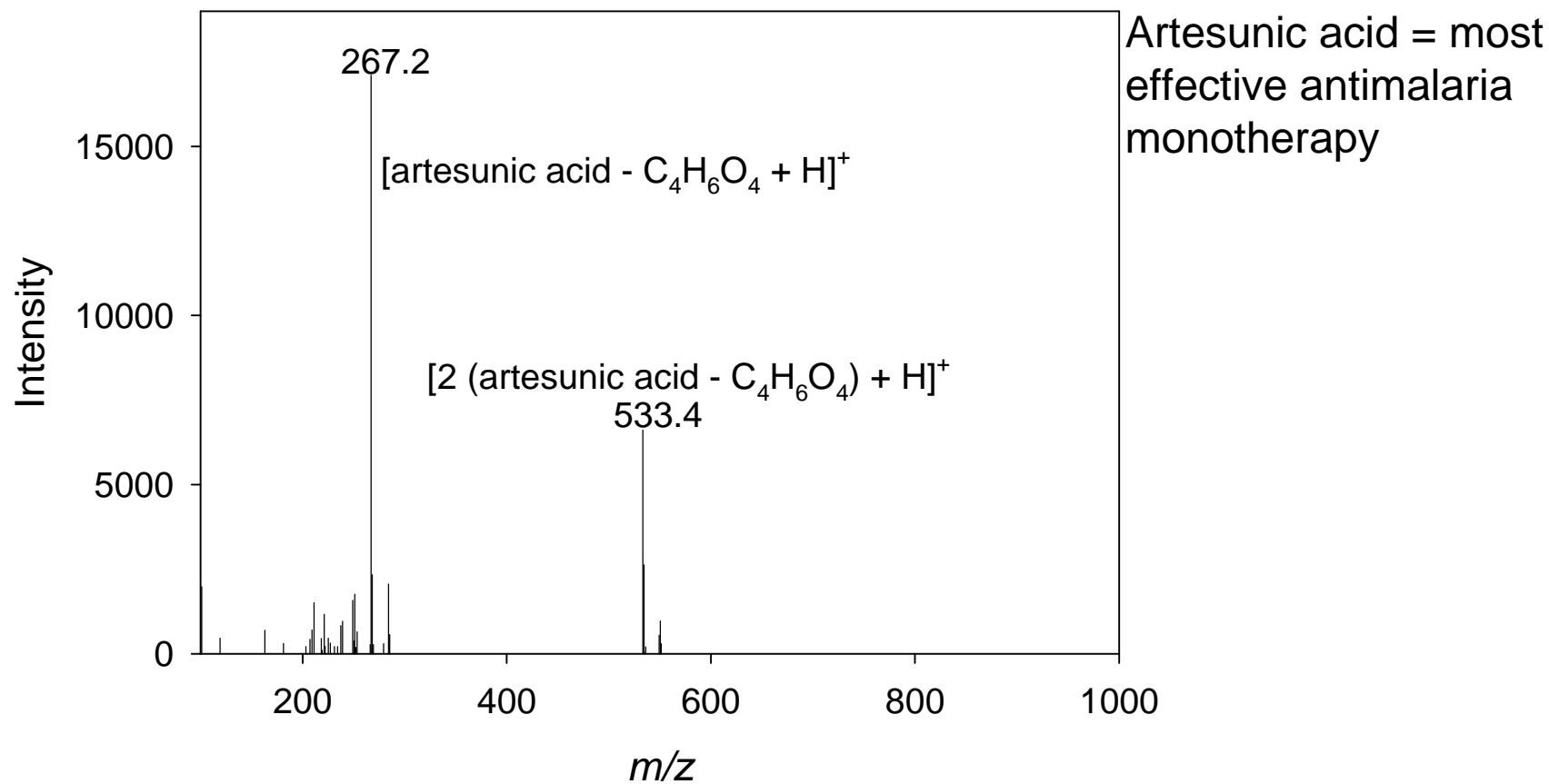
Template cutout 2mm/slot



# The Real World

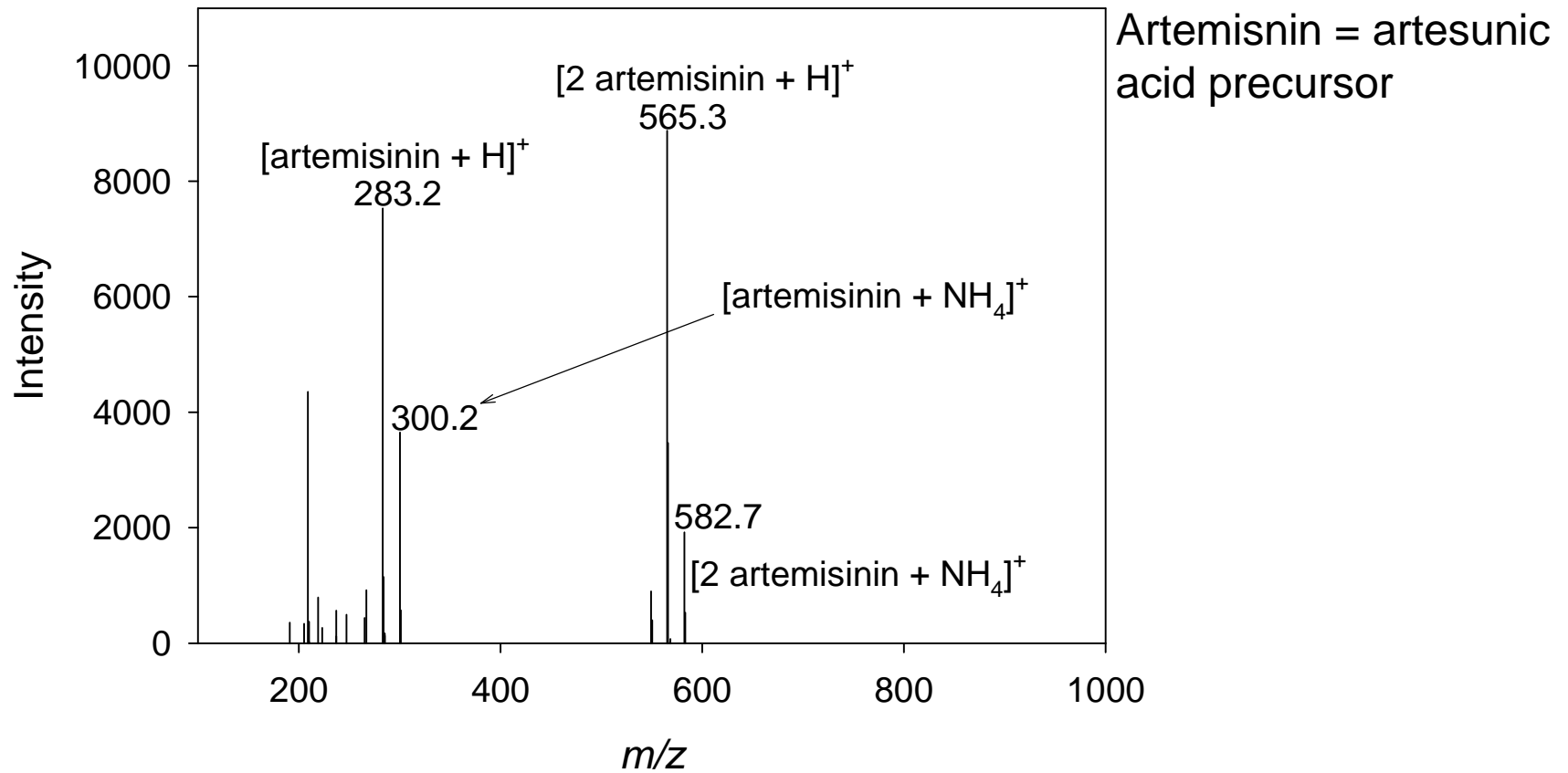
## DART-TOF-MS

### Genuine Artesunate Tablet



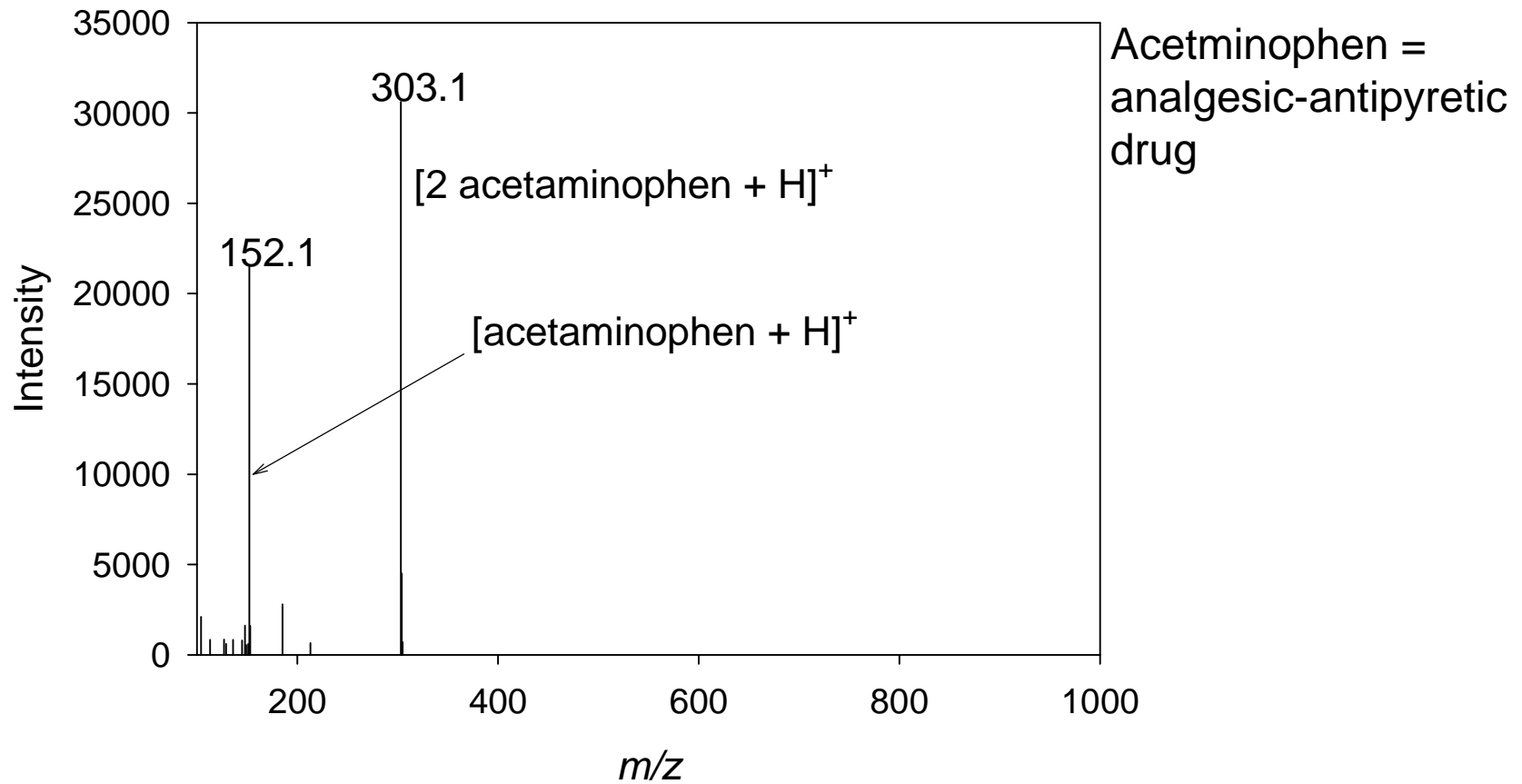
Data courtesy Facundo Fernandez, Georgia Institute of Technology. Samples collected by CODFIN ([www.codfin.org](http://www.codfin.org)).

# DART-TOF-MS: Artemisinin-containing Fake Tablet



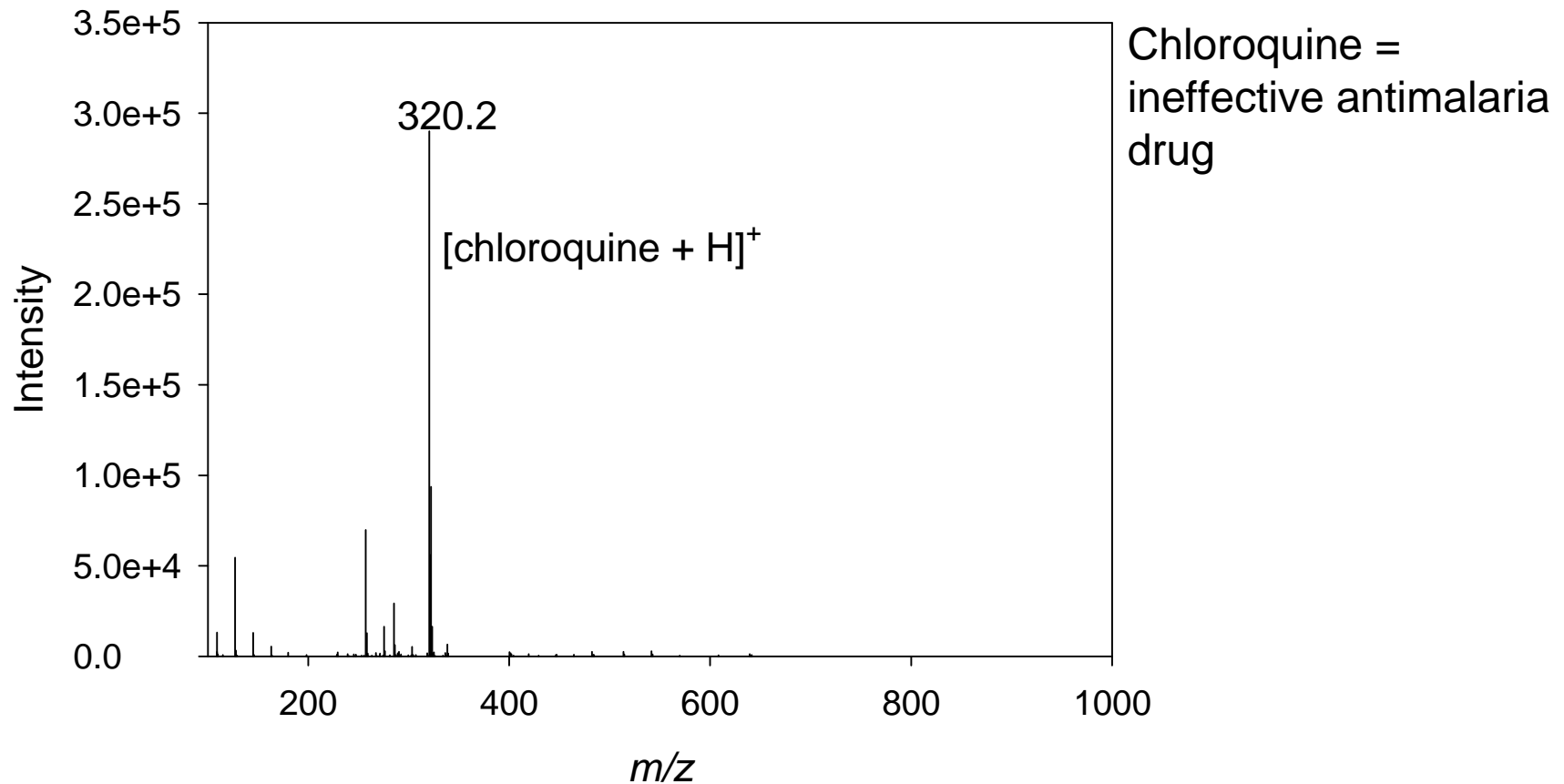
Data courtesy Facundo Fernandez, Georgia Institute of Technology. Samples collected by CODFIN ([www.codfin.org](http://www.codfin.org)).

# DART-TOF-MS: Acetaminophen-containing Fake Tablet



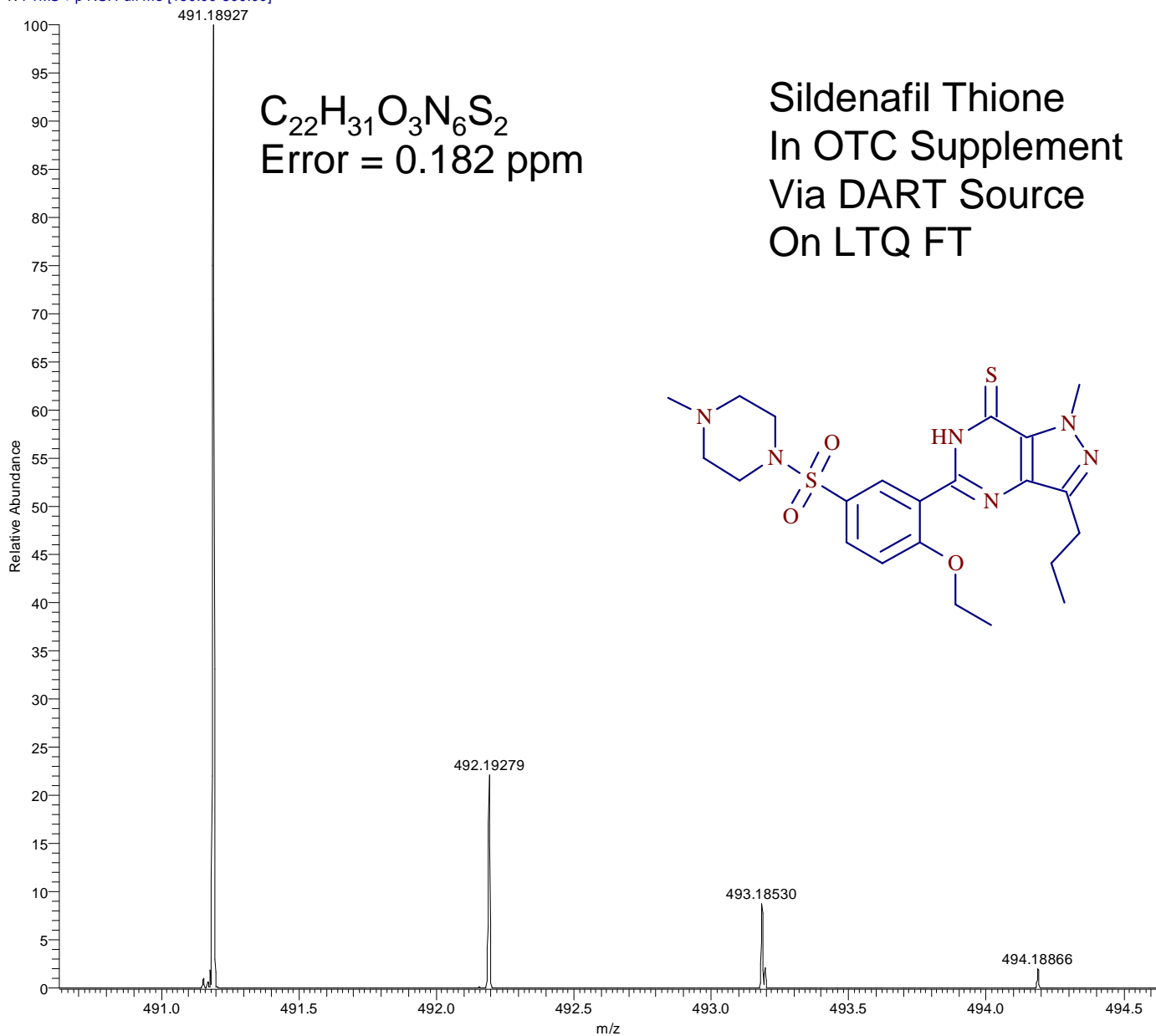
Data courtesy Facundo Fernandez, Georgia Institute of Technology. Samples collected by CODFIN ([www.codfin.org](http://www.codfin.org)).

# DART-TOF-MS: Chloroquine-containing Fake Tablet



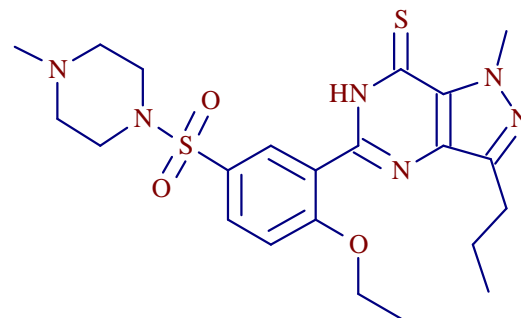
Data courtesy Facundo Fernandez, Georgia Institute of Technology. Samples collected by CODFIN ([www.codfin.org](http://www.codfin.org)).

silden\_thione\_a #1-52 RT: 0.01-0.81 AV: 52 NL: 2.87E6  
T: FTMS + p NSI Full ms [150.00-800.00]



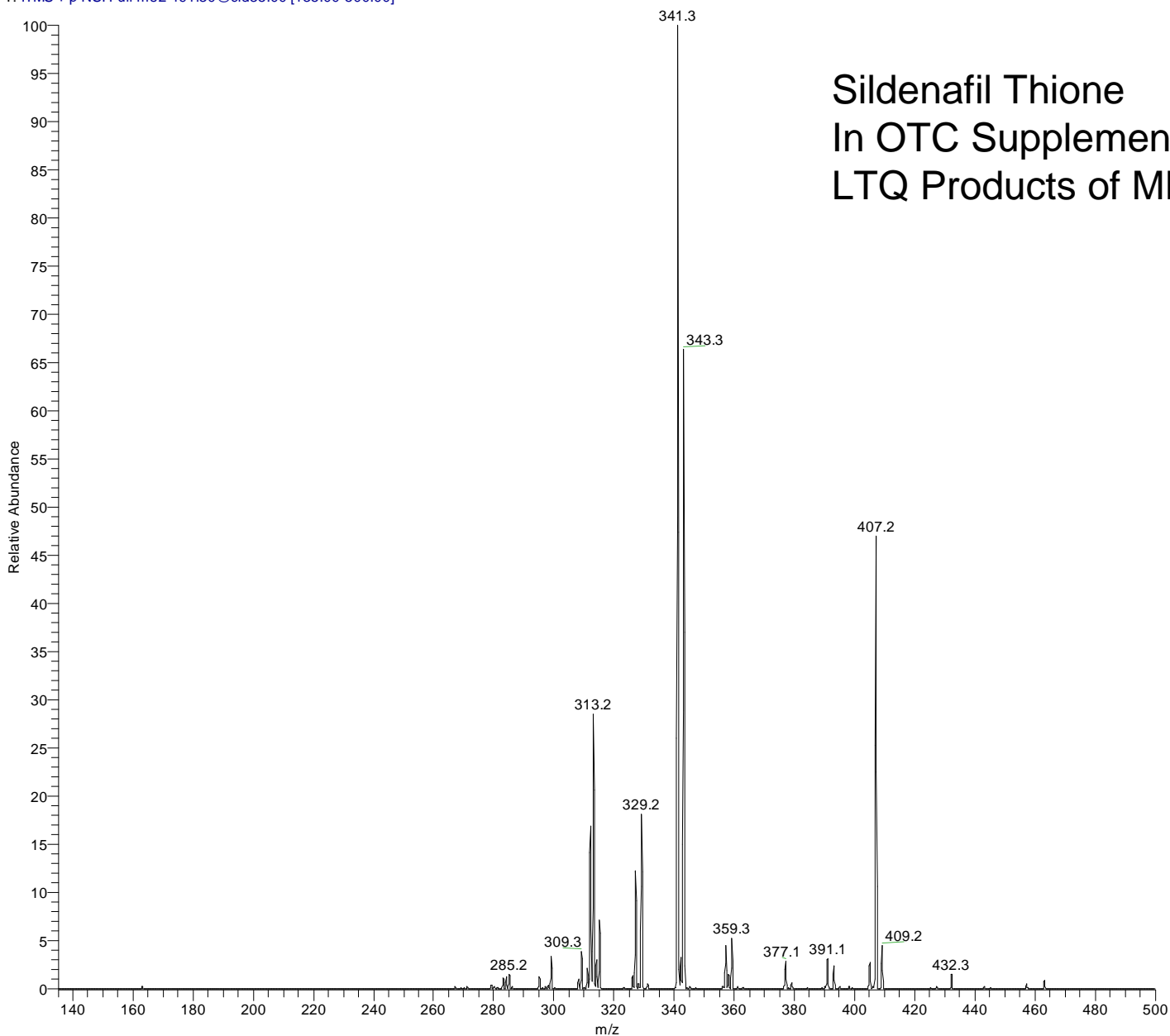
$C_{22}H_{31}O_3N_6S_2$   
Error = 0.182 ppm

Sildenafil Thione  
In OTC Supplement  
Via DART Source  
On LTQ FT



Data courtesy US FDA Forensics Laboratory

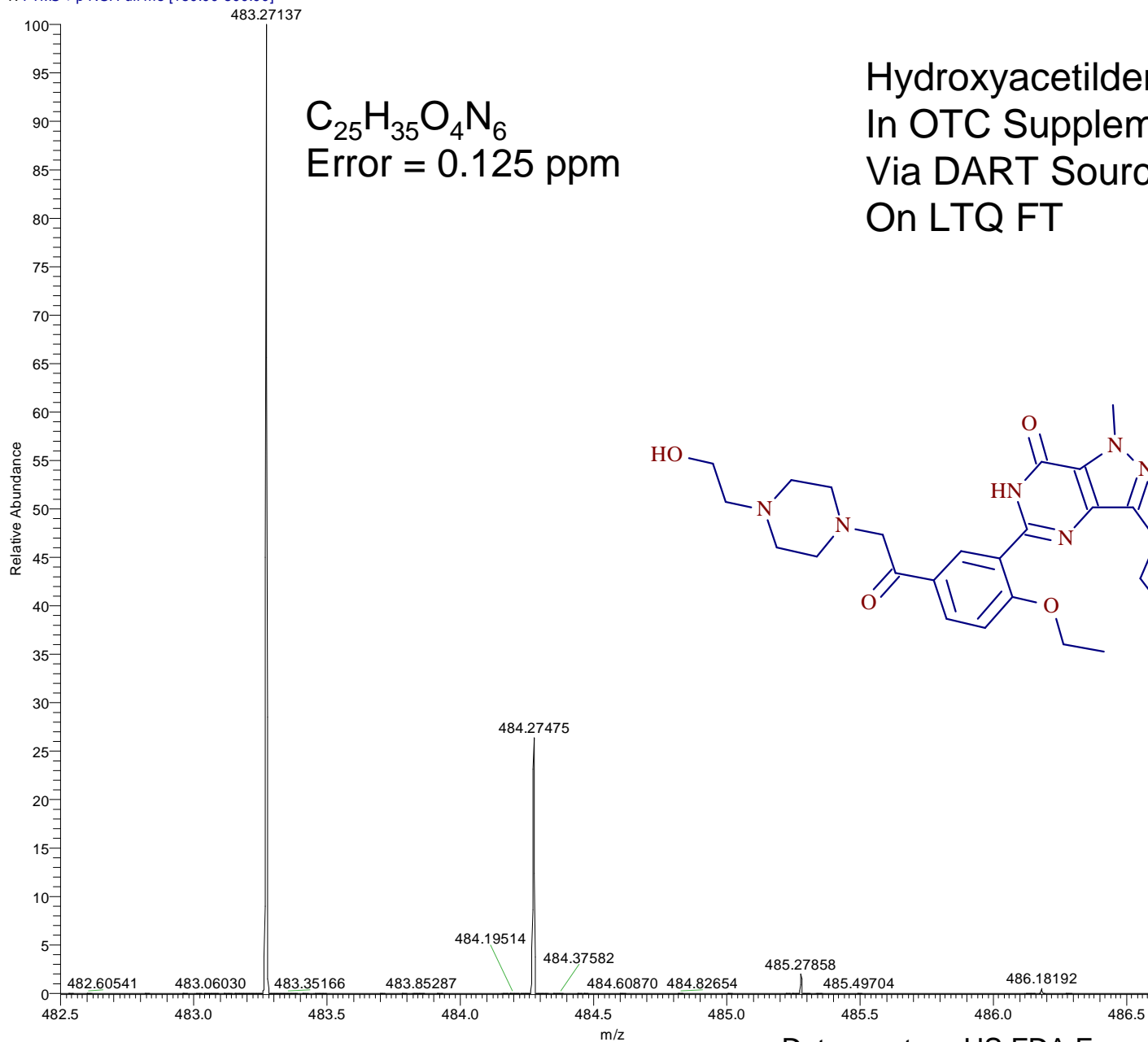
silden\_thione\_b #1-288 RT: 0.00-0.85 AV: 288 NL: 1.68E5  
T: ITMS + p NSI Full ms2 491.30@cid35.00 [135.00-500.00]



Sildenafil Thione  
In OTC Supplement  
LTQ Products of MH+

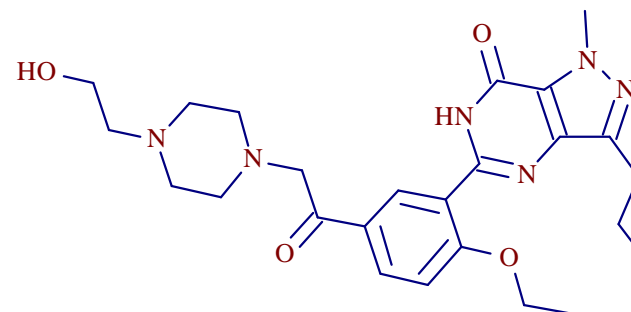
Data courtesy US FDA Forensics Laboratory

hydroxy\_acetilden\_a #1-54 RT: 0.01-0.89 AV: 54 NL: 9.50E4  
T: FTMS + p NSI Full ms [150.00-800.00]



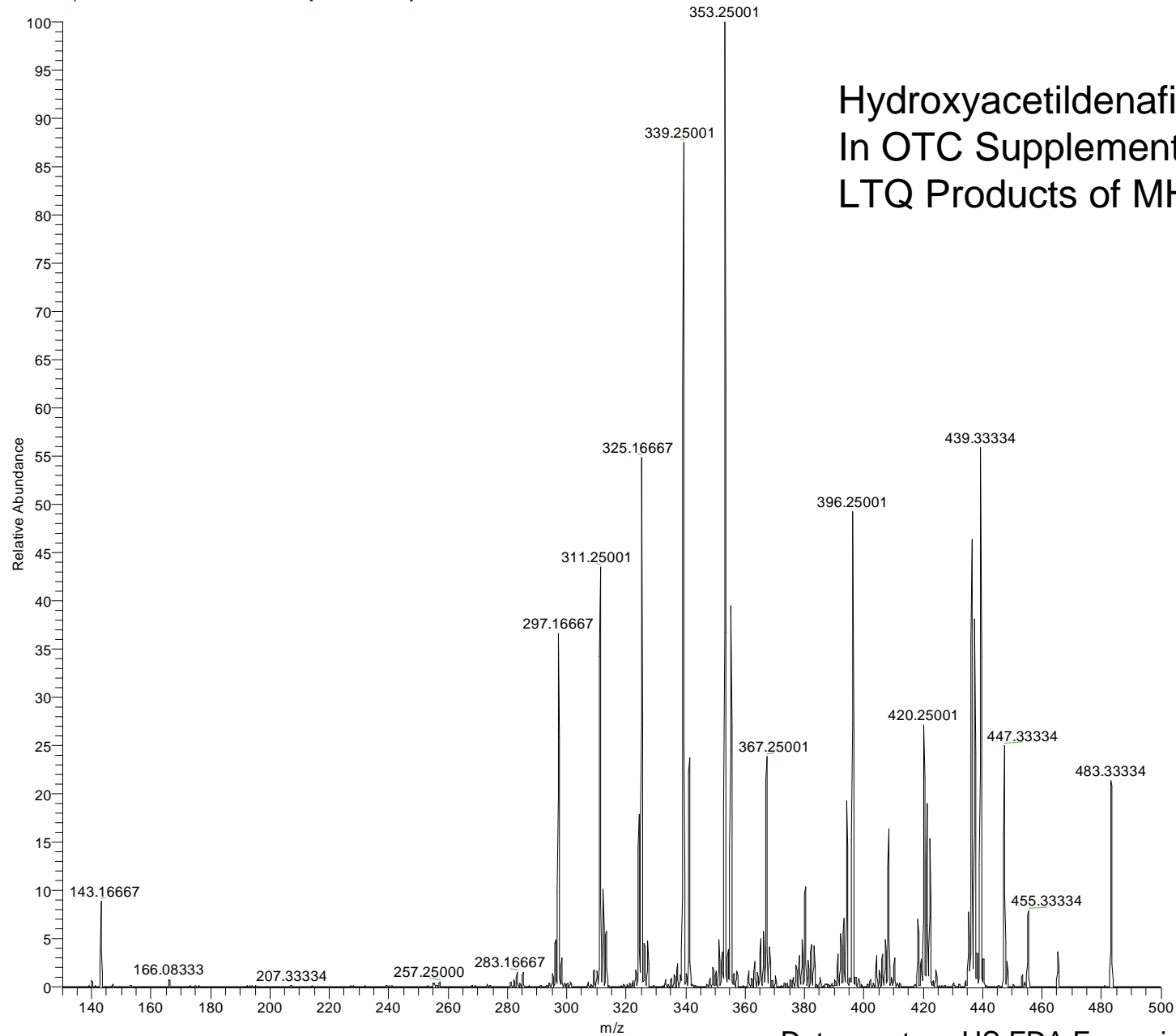
$C_{25}H_{35}O_4N_6$   
Error = 0.125 ppm

Hydroxyacetildenafil  
In OTC Supplement  
Via DART Source  
On LTQ FT



Data courtesy US FDA Forensics Laboratory

hydroxy\_acetilden\_b #1-163 RT: 0.00-0.75 AV: 163 NL: 6.10E2  
T: ITMS + p NSI w Full ms2 483.30@cid35.00 [130.00-500.00]



Data courtesy US FDA Forensics Laboratory

# Conclusions

- Direct analysis of solid samples offers practical approach for detection of genotoxic materials
- Development of methods critical to success
- Temperature and exposure time depend on formulation and excipients
- Components present in low concentration can be detected using a solid analytical approach
- Problems are being identified and investigated