# LC/MS

## Why is it the fastest growing analytical technique ?

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# Discussion topics

- Evolution of LC/MS
- Advantages of API
- Why should I use LC/MS ?
- LC/MS markets

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# Evolution of LC/MS interfaces

1970s to Present

Moving belt interface (EI and CI, library searchable)

Dynamic FAB (low flow rates, very fiddly)

TSP ionisation (first widely used LC/MS interface)

Atmospheric Pressure Ionisation (ESI and APCI)

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# Advantages of API

Soft ionisation (gives the molecular weight)

Sensitive (low pg amounts routinely)

Robust, simple, run routinely 24 hr/day

Wide range of flow rates (nanospray to analytical)

Wide range of applications (drugs, proteins)

Wide range of industries

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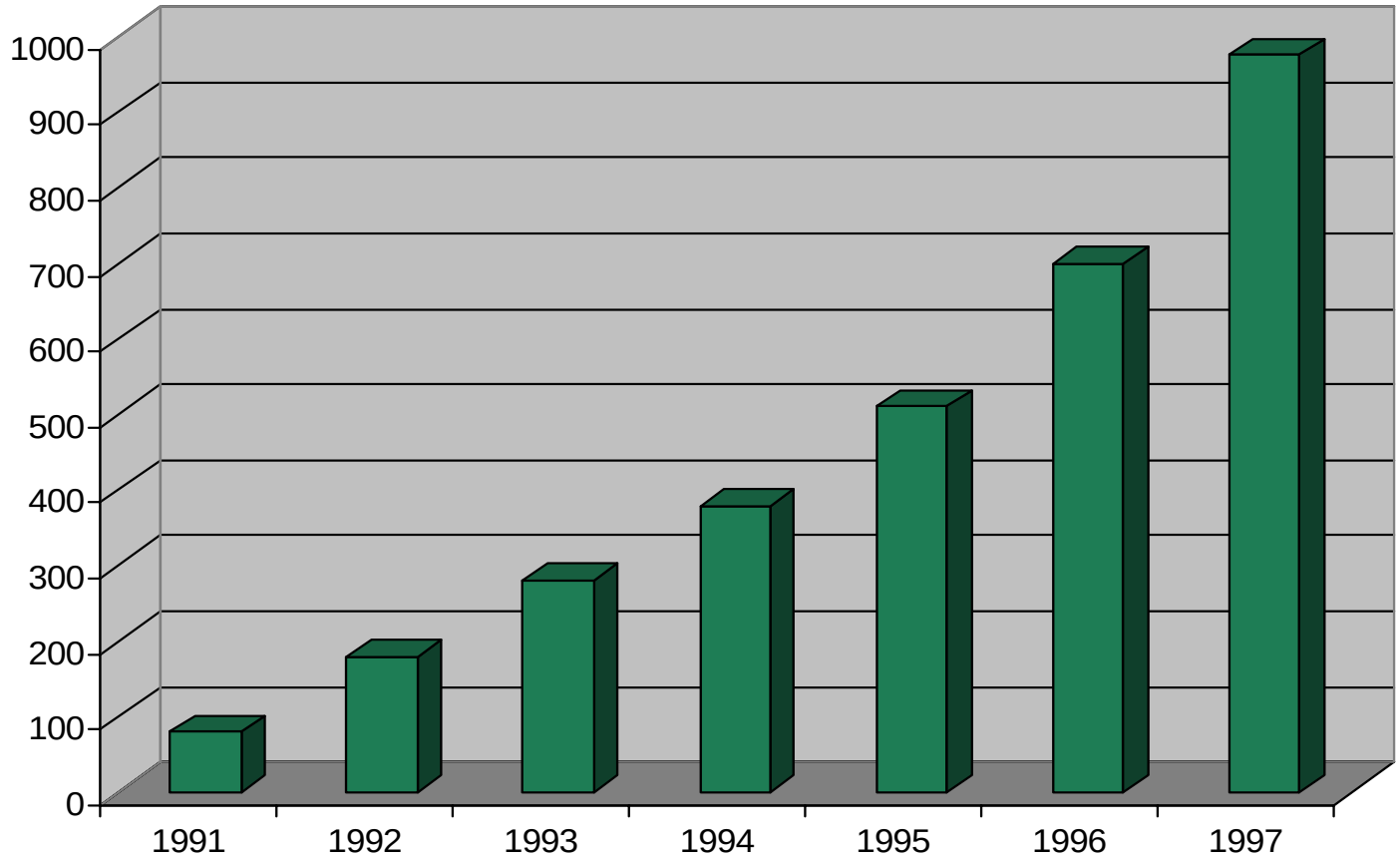
# API Publications




Halket JM and Down S, LC/MS Update, HD Science, Nottingham

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# LC/MS for shorter analysis times

Example :

MS vs photo diode array detector for the analysis of steroids

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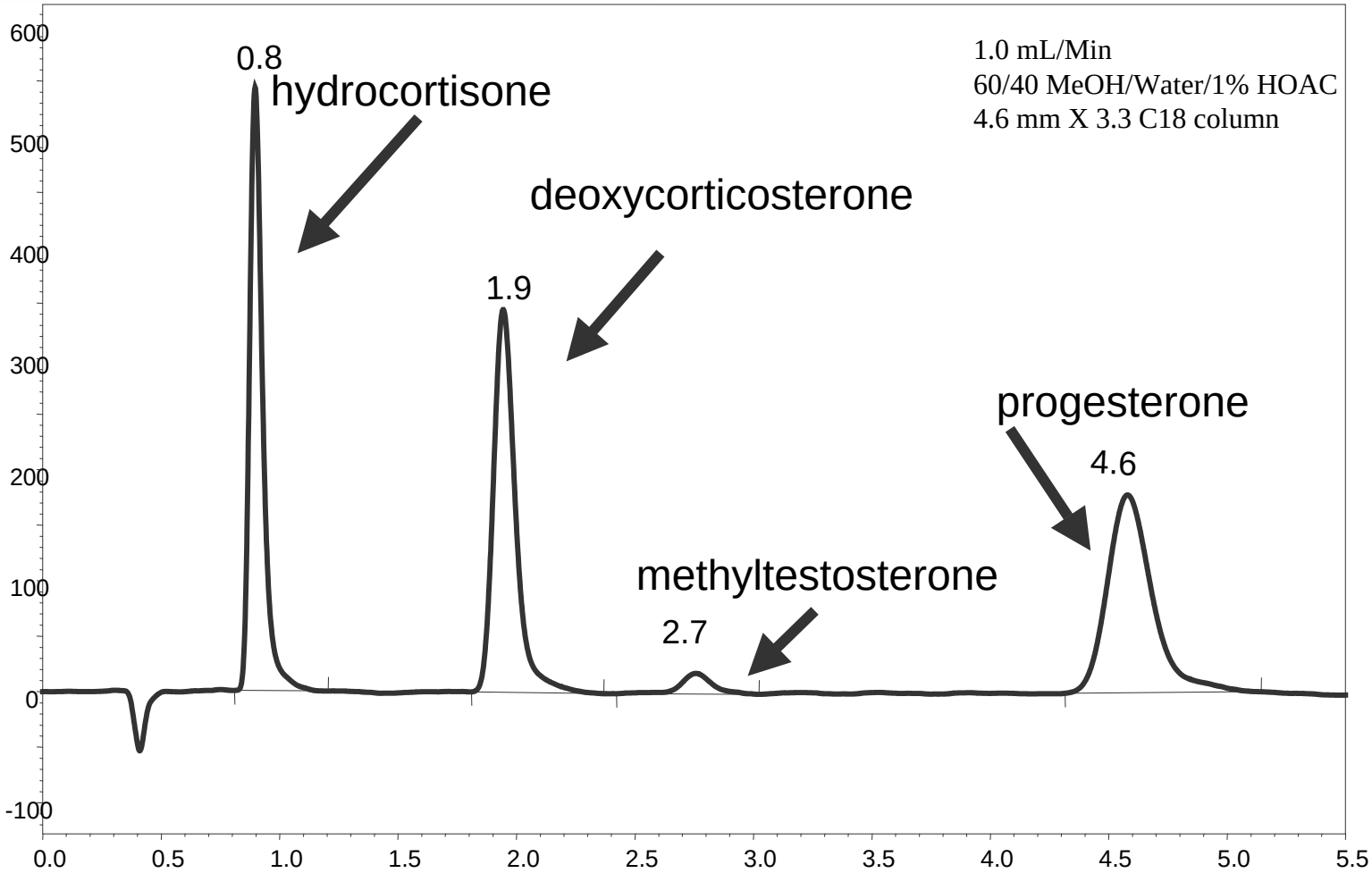
# Steroid standards, 25ng injected

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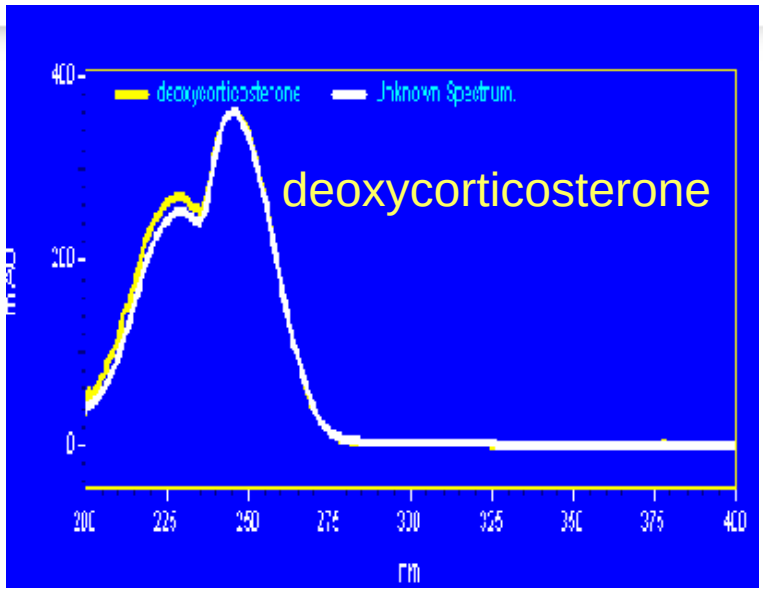
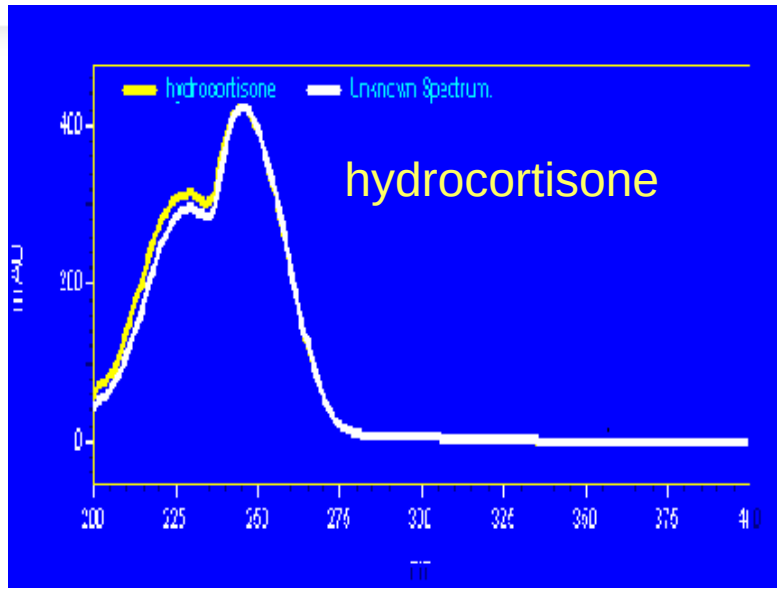
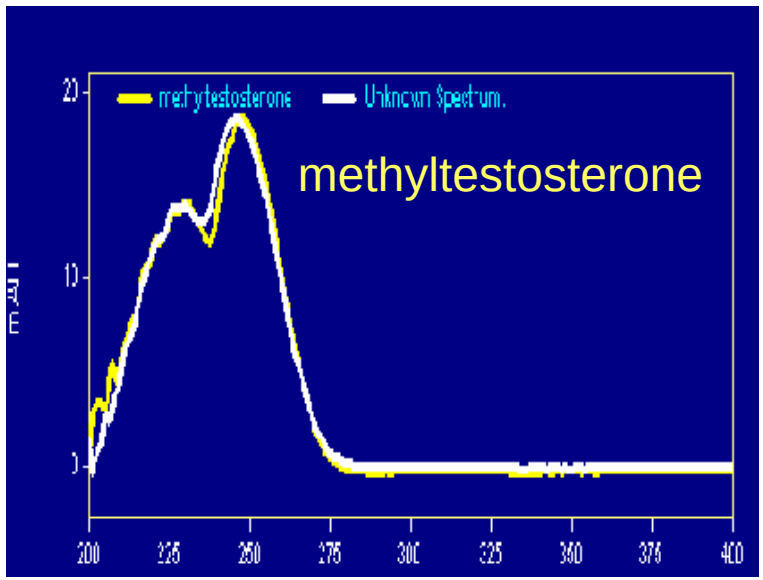
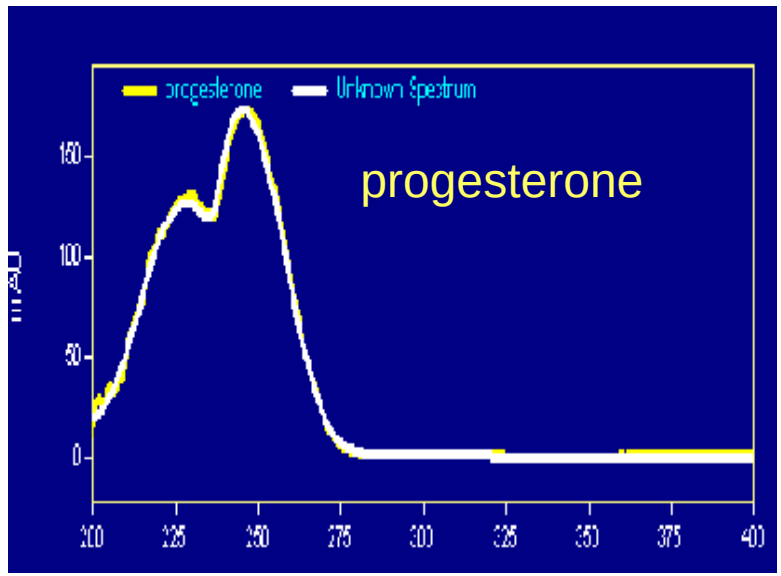
# PDA spectra of standard steroids

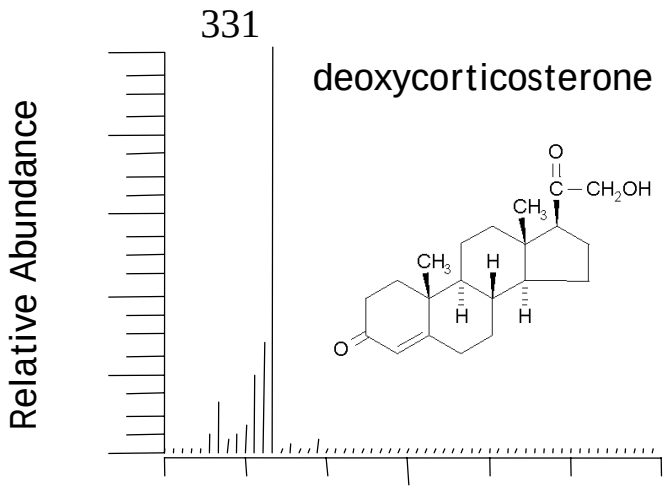


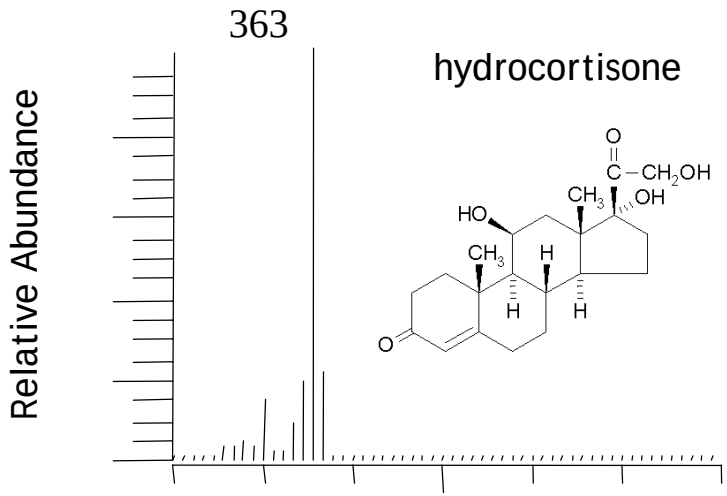



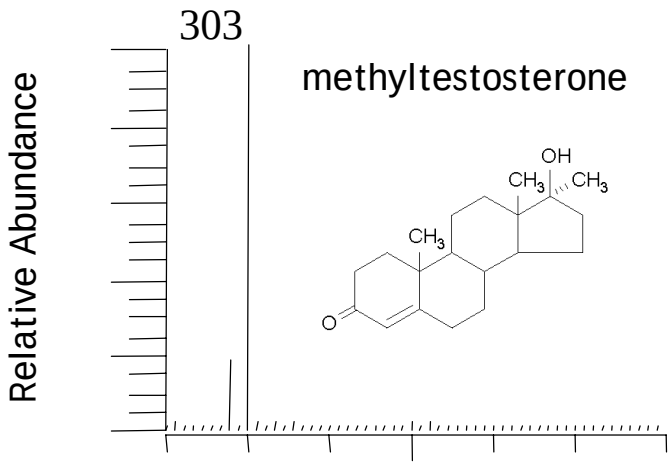



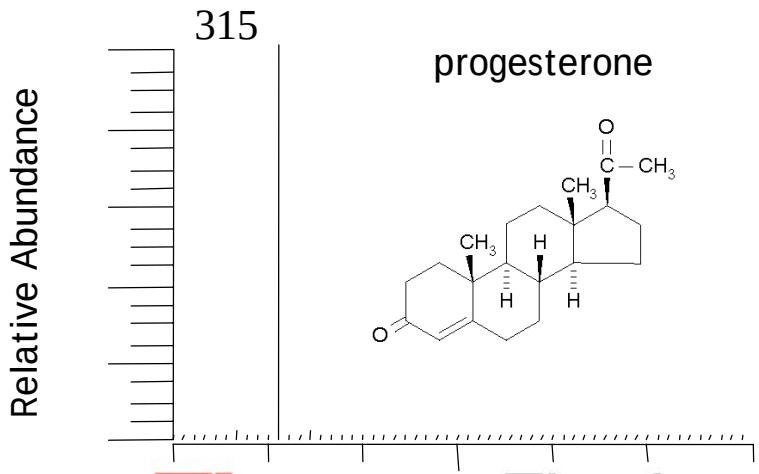



# MS Spectra of steroids

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# LC/MS for shorter analysis times

What happens if we speed up the chromatography ?

(from 60/40 to 90/10 MeOH/Water)

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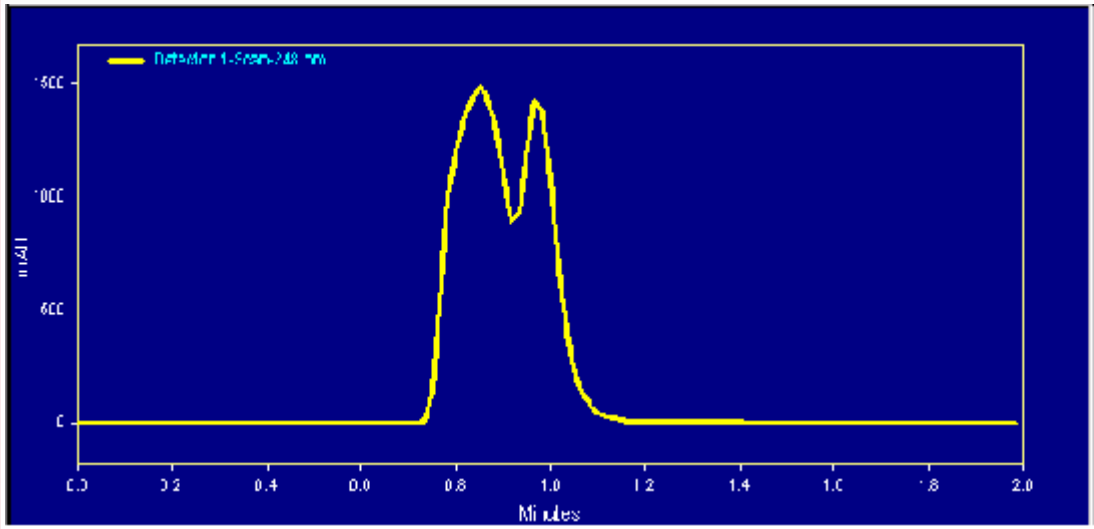
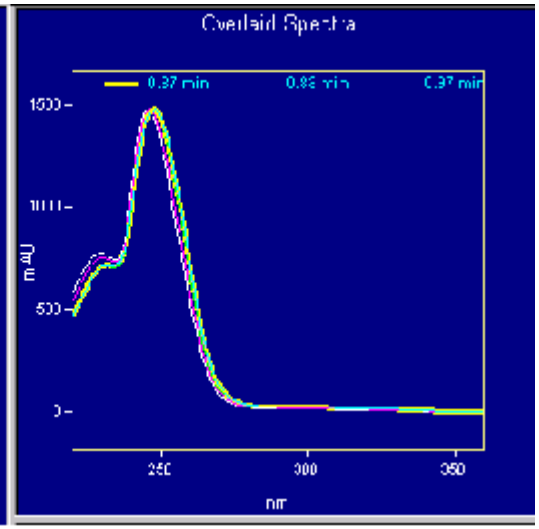
# Detection by UV




Steroids coelute

No distinguishing UV spectra

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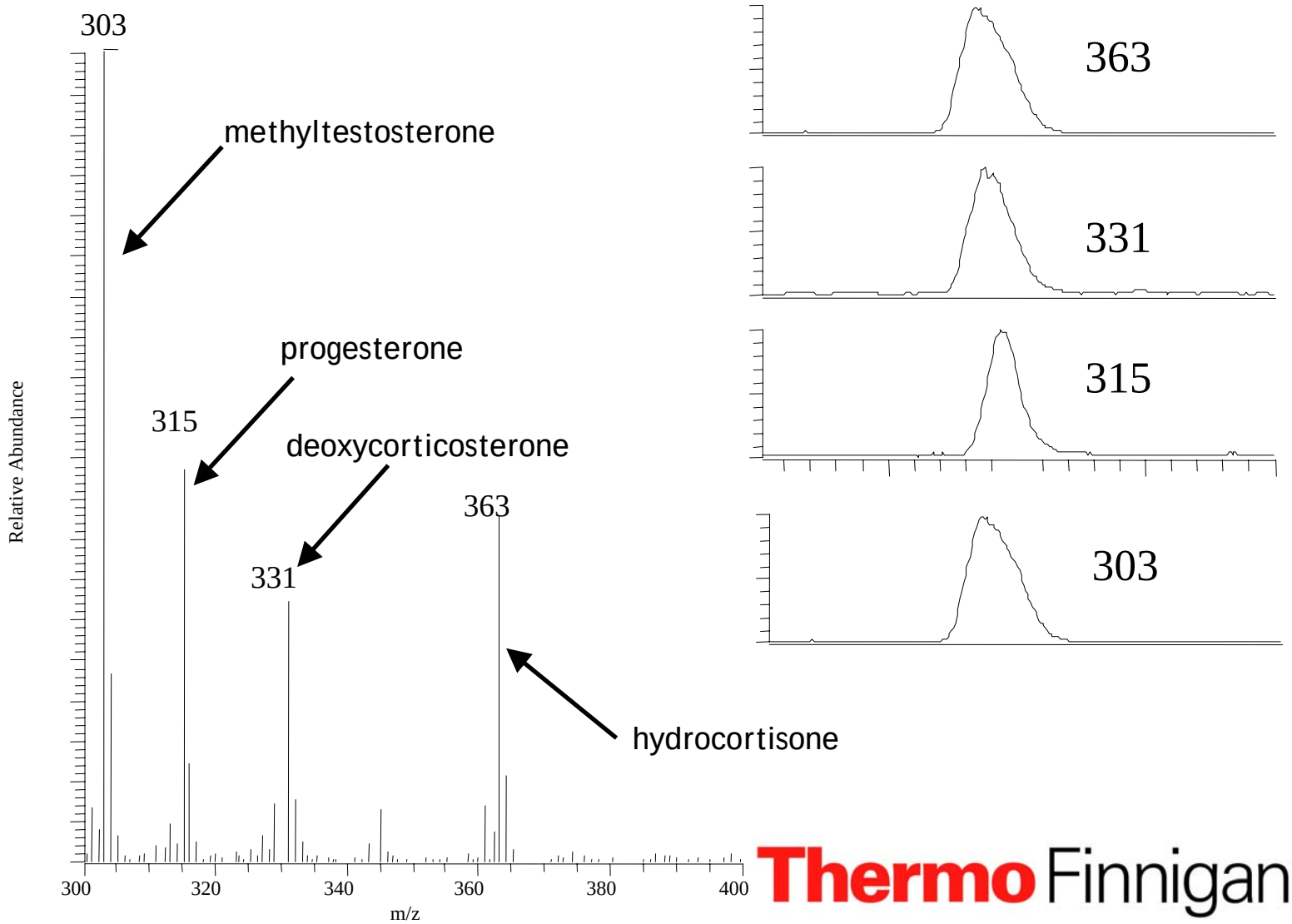
# Detection by MS

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# LC/MS shorter run times

- Changing from 6 to 2 min / sample means :
  - 10 samp / hr → 30 samp / hr
  - 80 samp / day → 240 samp / day
  - 20,000 samp / yr → 60,000 samp /yr

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# Did This Horse Win The Race

*Legally ?*

A wide variety of drugs are dosed to horses to enhance performance during racing.

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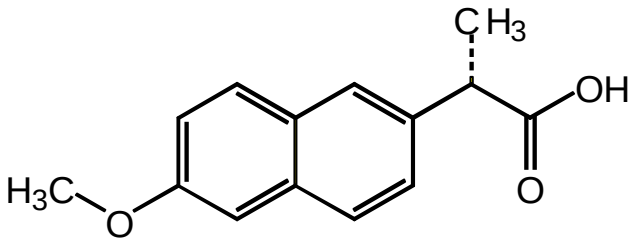
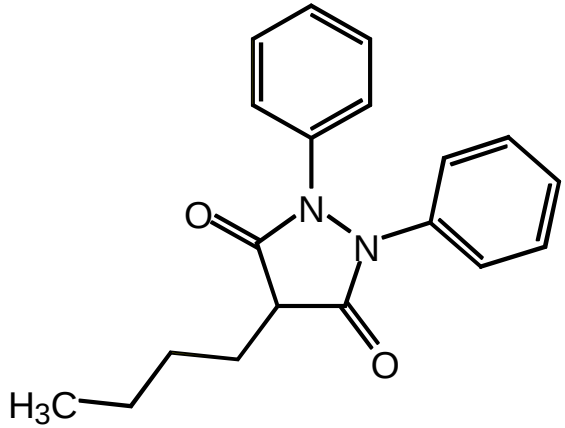
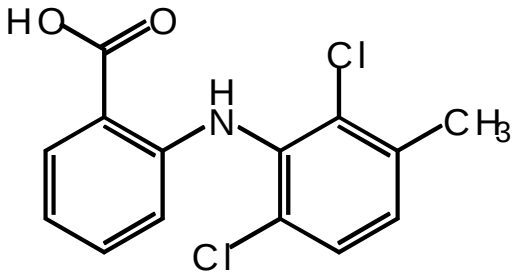
# Frequently used analgesics



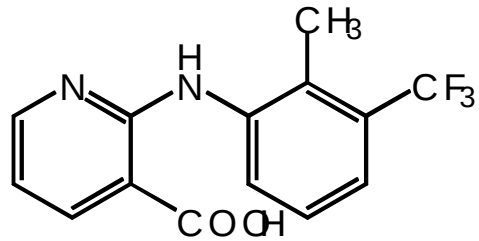

Naproxen




Phenylbutazone




Meclofenamic Acid




Flunixin

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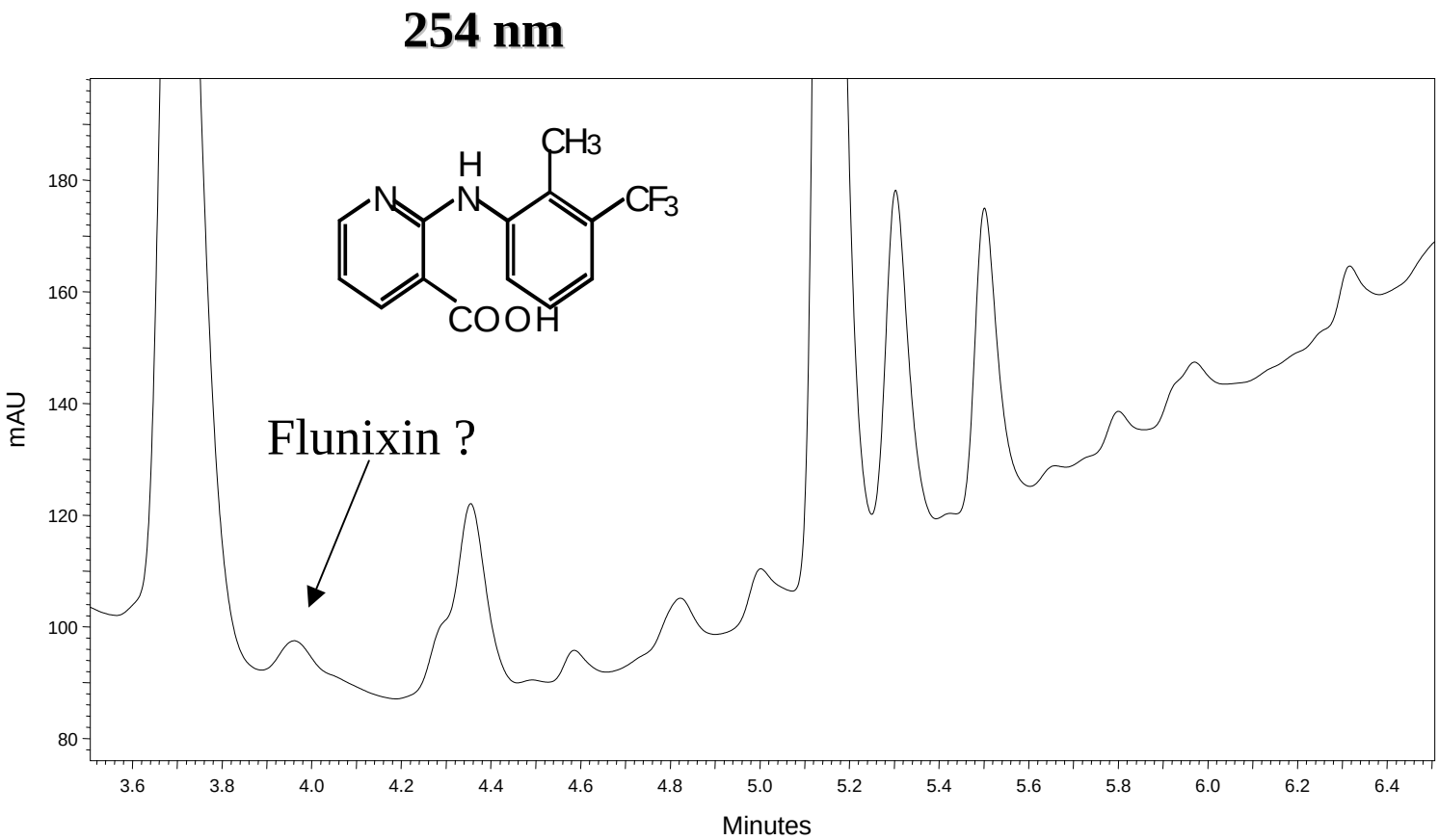
# Is this peak Flunixin ?

*It has the correct retention time by UV*

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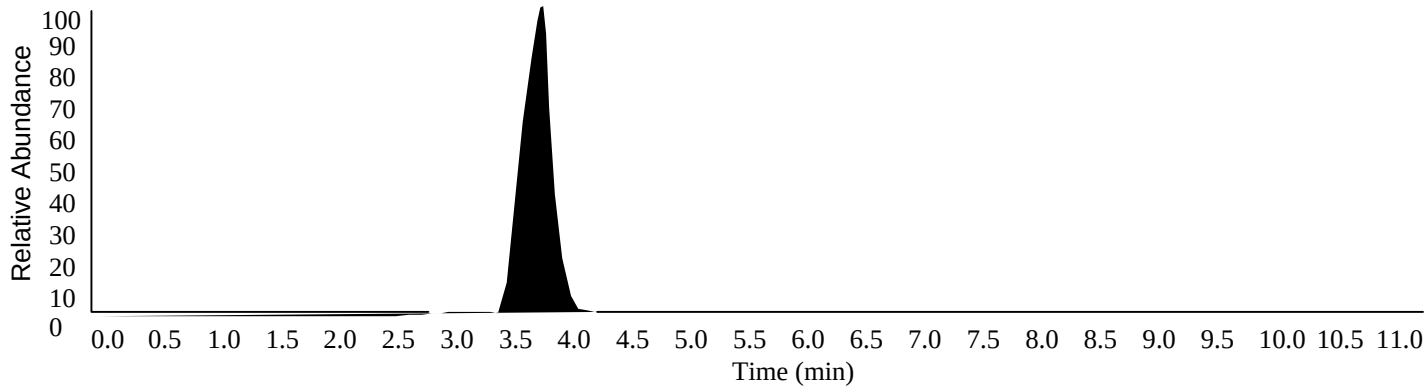
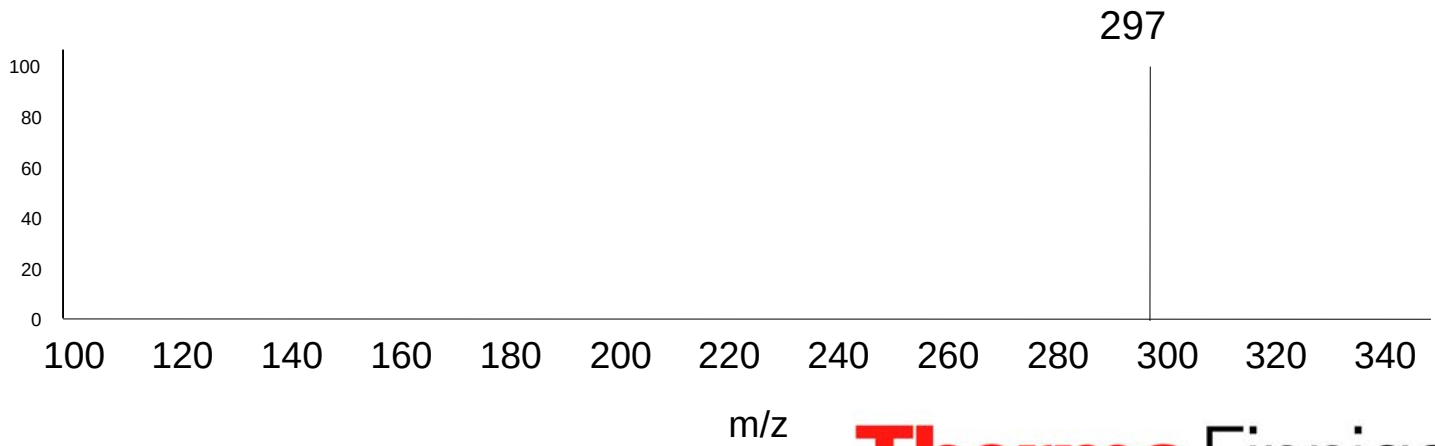
# LC/MS confirms it to be Flunixin

Flunixin Full Scan MS

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# Why should I use LC/MS ?

- Higher sample throughput
  - $
- Shorter method development
  - $
- Better sensitivity
  - environmental, legislation
- Unequivocal ID
  - safety

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# LC/MS markets

Who uses LC/MS ?

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# LC/MS in the pharmaceutical market

- Drug discovery
  - molecular weight, structural
  - open access
  - combinatorial chemistry
- Metabolism
  - structural identification and quantification of metabolites
- Toxicology
  - quantitation

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# LC/MS in the pharmaceutical market

- Pharmacokinetics
  - quantitation, sensitivity,precision and accuracy
  - pre-clinical and clinical studies
- Formulation
  - structural, degradation products
- QC & Production
  - quantitation
  - ID of impurities & unexpected peaks

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# LC/MS in pharmaceutical related markets

- Contract research organisations
  - quantitation, pre-clinical & clinical trials
  - structural studies
- Generic drug companies
  - QC and production

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# LC/MS in the biotechnology market

- Protein characterisation
  - molecular weight, (3D structure)
- Proteomics
  - rapid peptide sequencing
  - post translational modifications
- QC
  - confirm sequence & impurities

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# LC/MS in the biotechnology market

- Nucleotides
  - molecular weight, sequence
- Carbohydrates
  - molecular weight, sequence

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# LC/MS in the agrochemical market

- Compound discovery
- Metabolism
- Toxicology
- Pharmacokinetics
- QC and production

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# LC/MS in industrial markets

- Organometallics
  - structure
- Detergents
  - QC, competitors products
- Polymers
  - molecular weight, structure

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# LC/MS in the environmental market

- Water
  - ID and quantitation of pollutants
- Food
  - chemical contaminants
  - natural toxins
- Animal feeds
  - contaminants, illegal substances

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# LC/MS in the forensic market

- Scene of crime
  - illegal substances, toxic agents
- Horse race doping
  - illegal substances
- Explosives
- Drugs of abuse
  - urine, hair, banknotes

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# LC/MS in clinical markets

- Replace immuno assays
- Drugs of abuse

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# LC/MS in academia

- Related to all of the above
- Fundamental research
- Teaching

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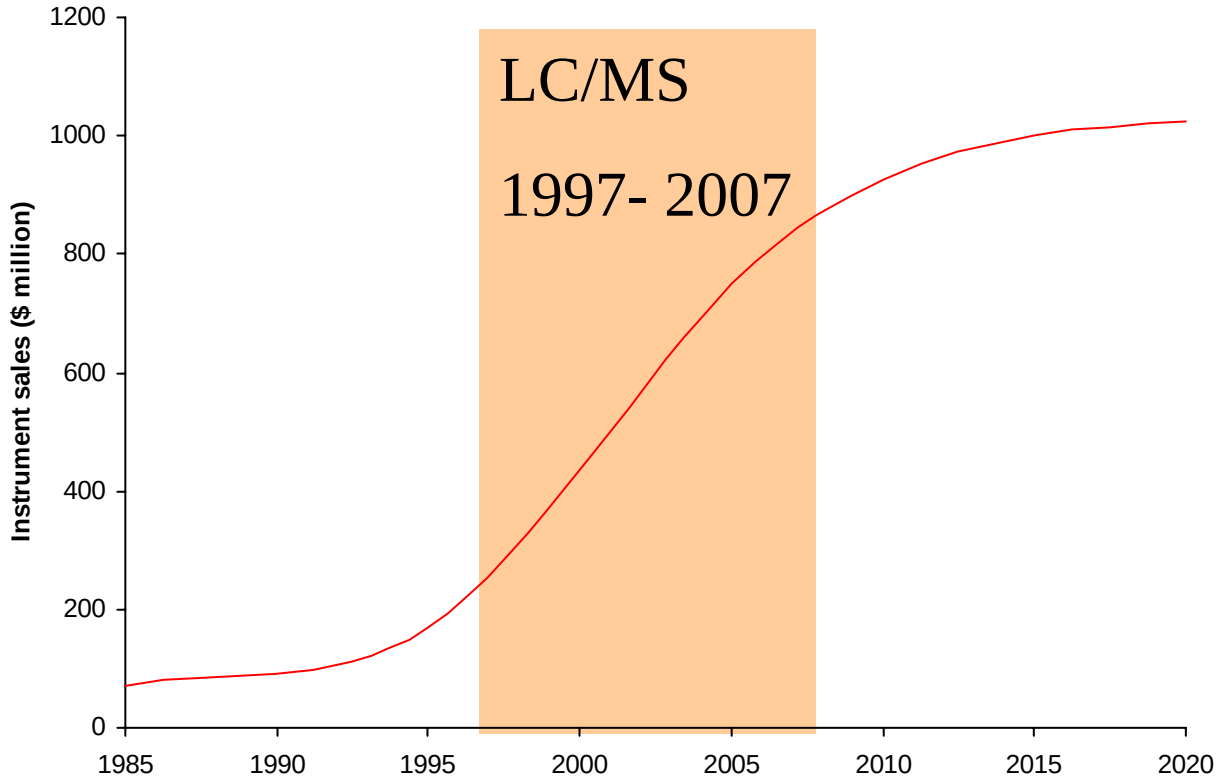
# Predicted market for LC/MS systems




Willoughby R, Sheenan E and Mitrovich S, "A Global View of LC/MS", Global View Publishing (1998)

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# Conclusion

- LC/MS is an established technique
- Market is growing rapidly
- LC/MS moving out of the specialised labs into every department
- Wide variety of LC/MS analyser types
- Non-specialist users

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