

A vertical bar on the left side of the slide, transitioning from red at the top to dark blue at the bottom.

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

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)

Advantages of API

Soft ionisation (gives the molecular weight)

Sensitive (low pg amounts routinely)

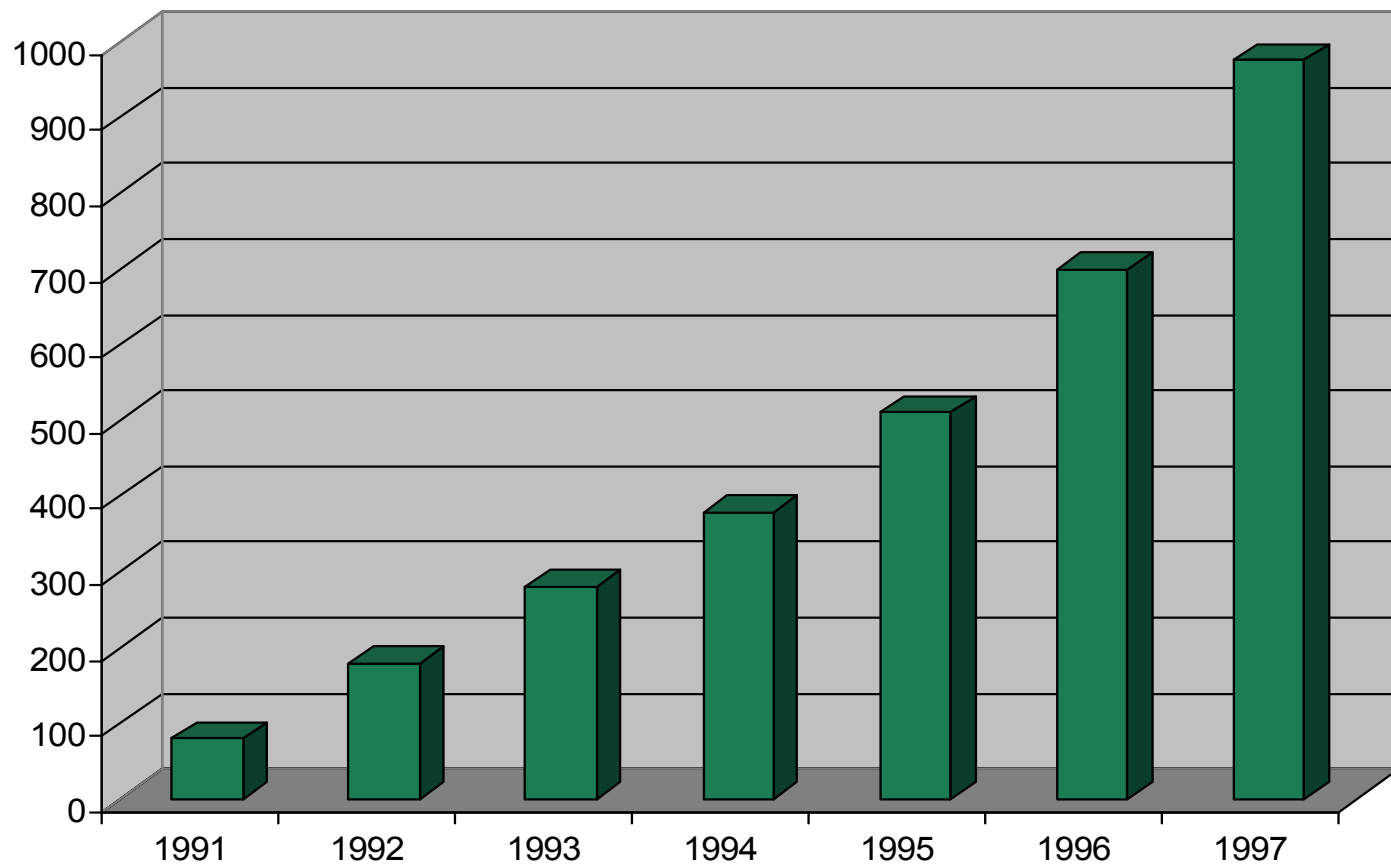
Robust, simple, run routinely 24 hr/day

Wide range of flow rates (nanospray to analytical)

Wide range of applications (drugs, proteins)

Wide range of industries

API Publications



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

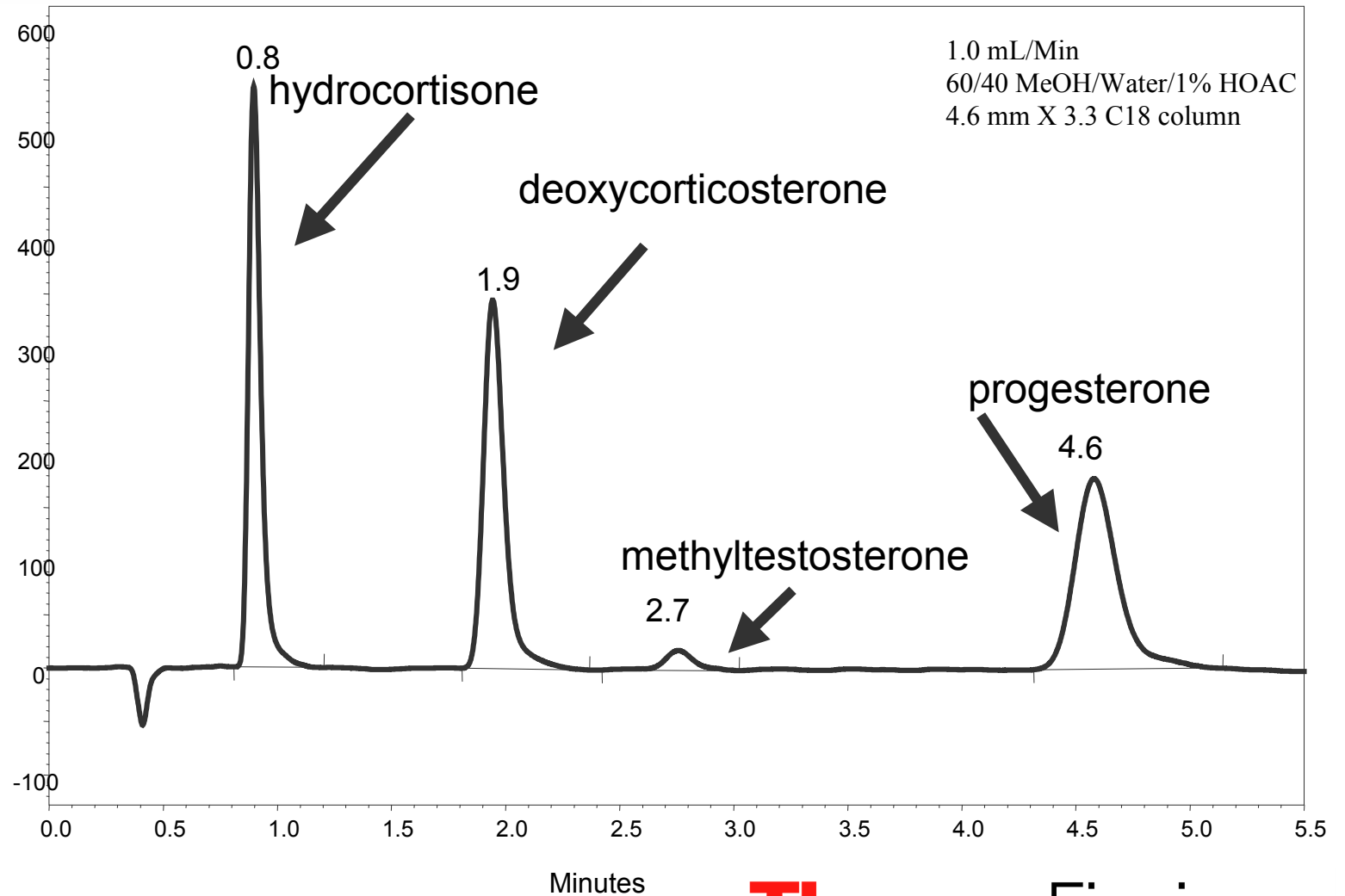
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LC/MS for shorter analysis times

Example :

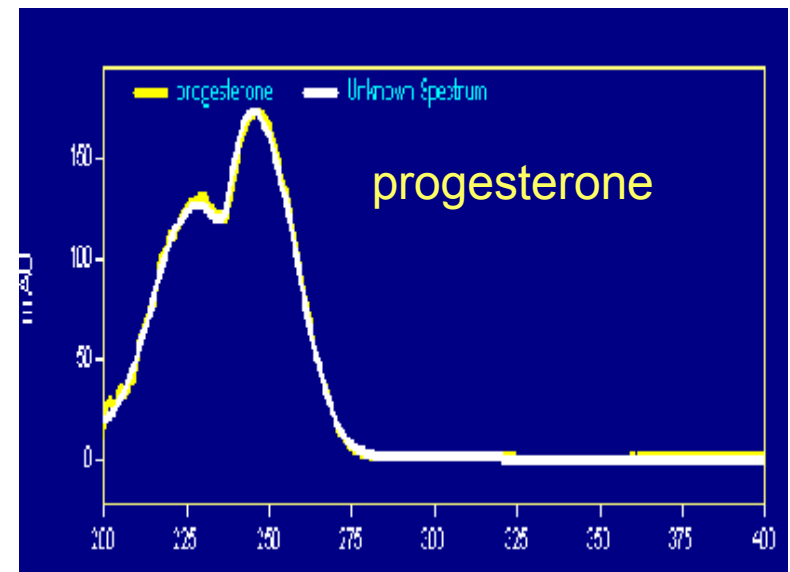
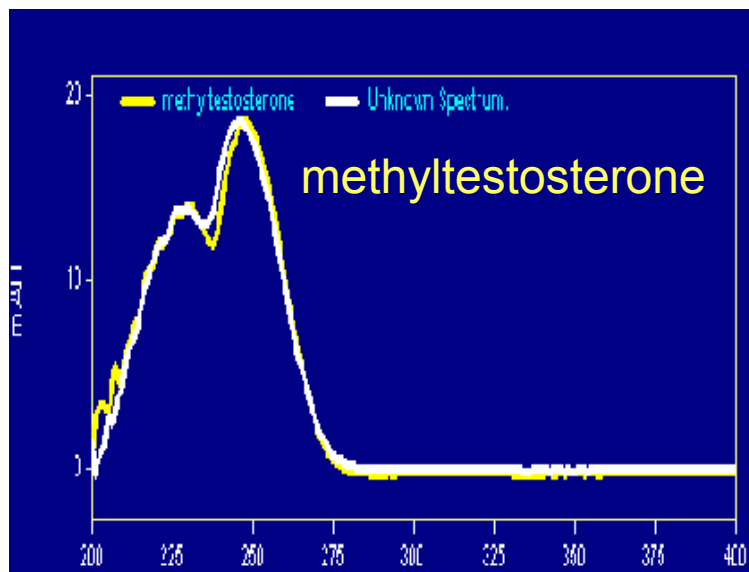
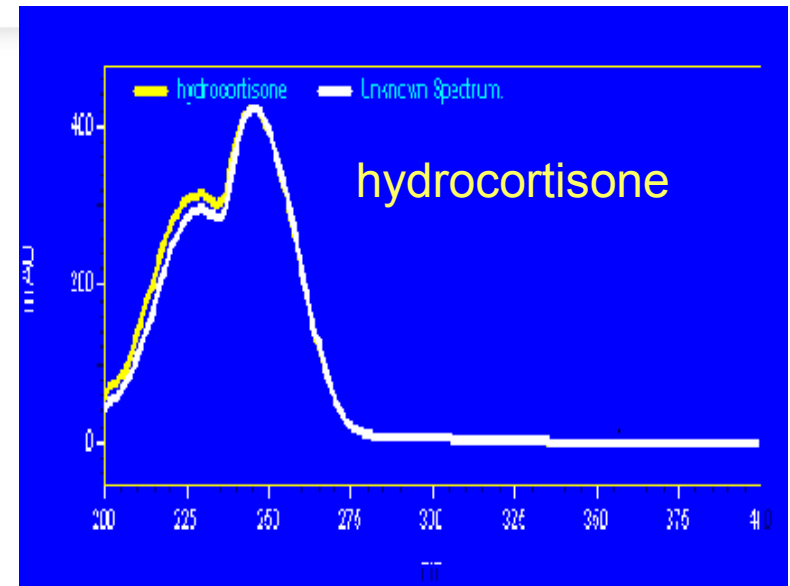
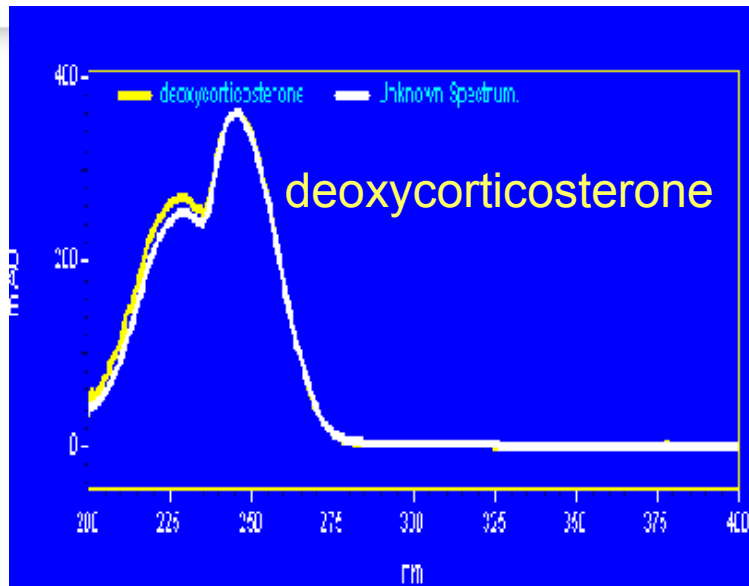
MS vs photo diode array detector for the
analysis of steroids

Steroid standards, 25ng injected

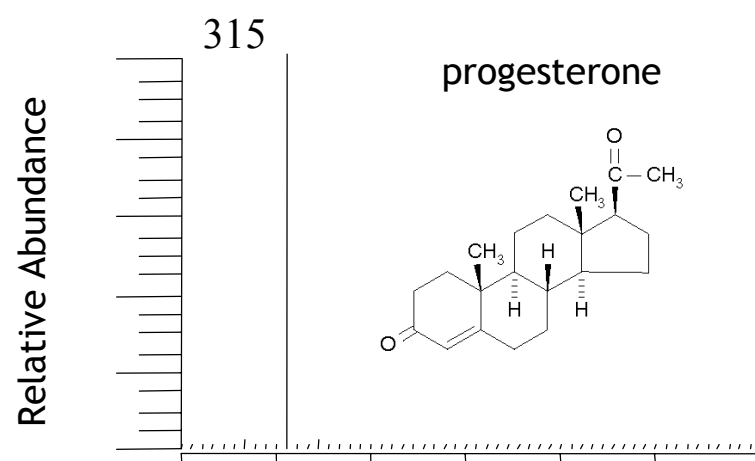
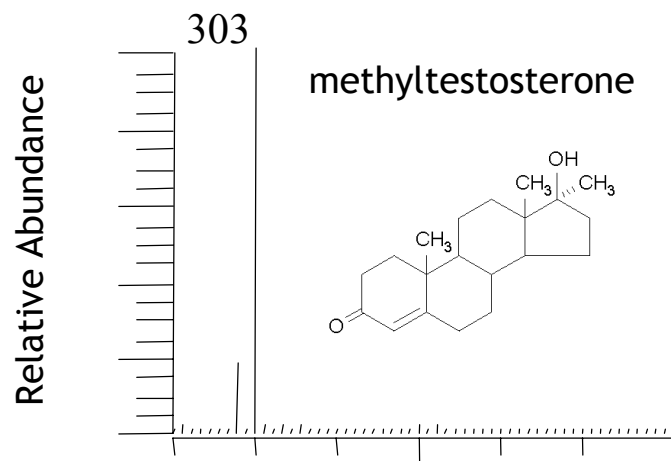
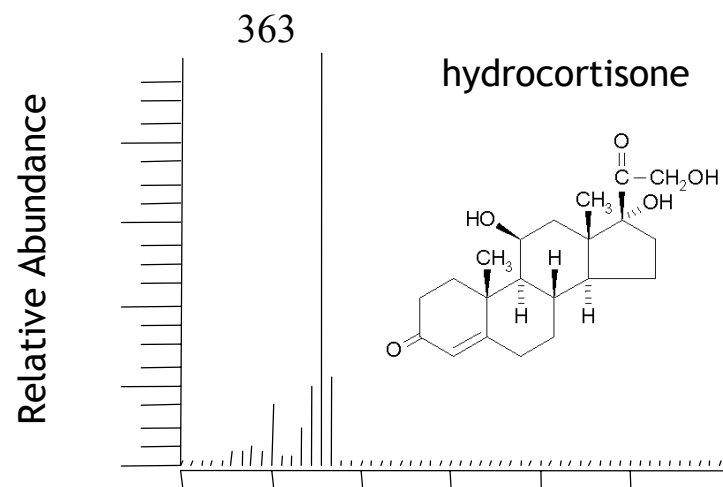
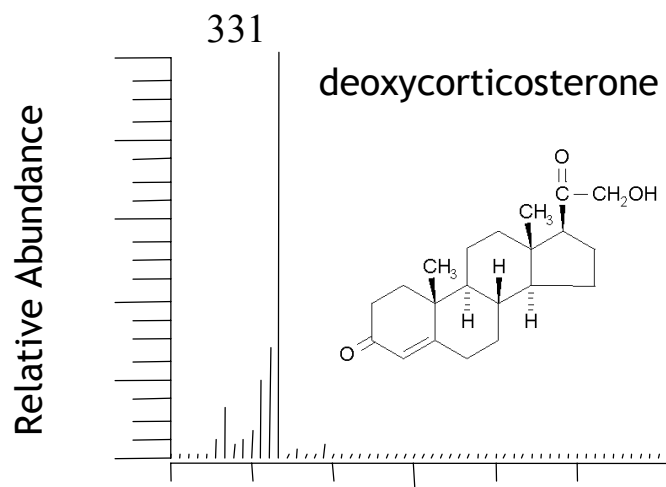


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PDA spectra of standard steroids



MS Spectra of steroids



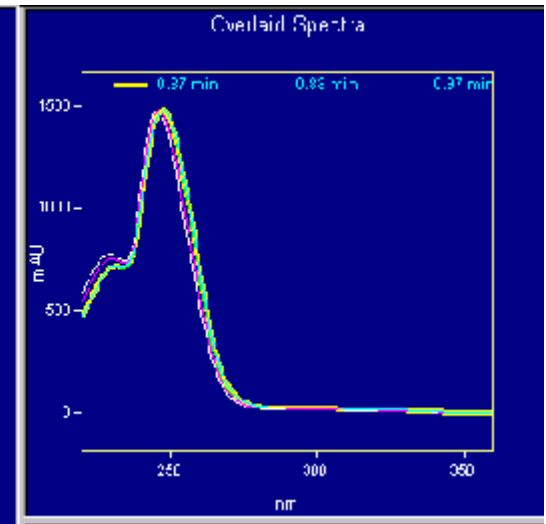
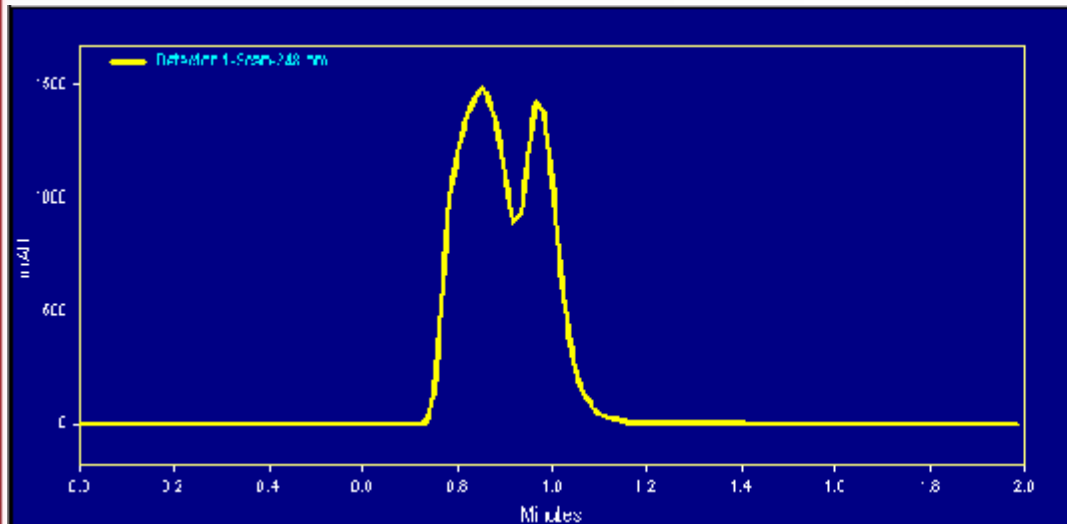
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LC/MS for shorter analysis times

What happens if we speed up the chromatography ?

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

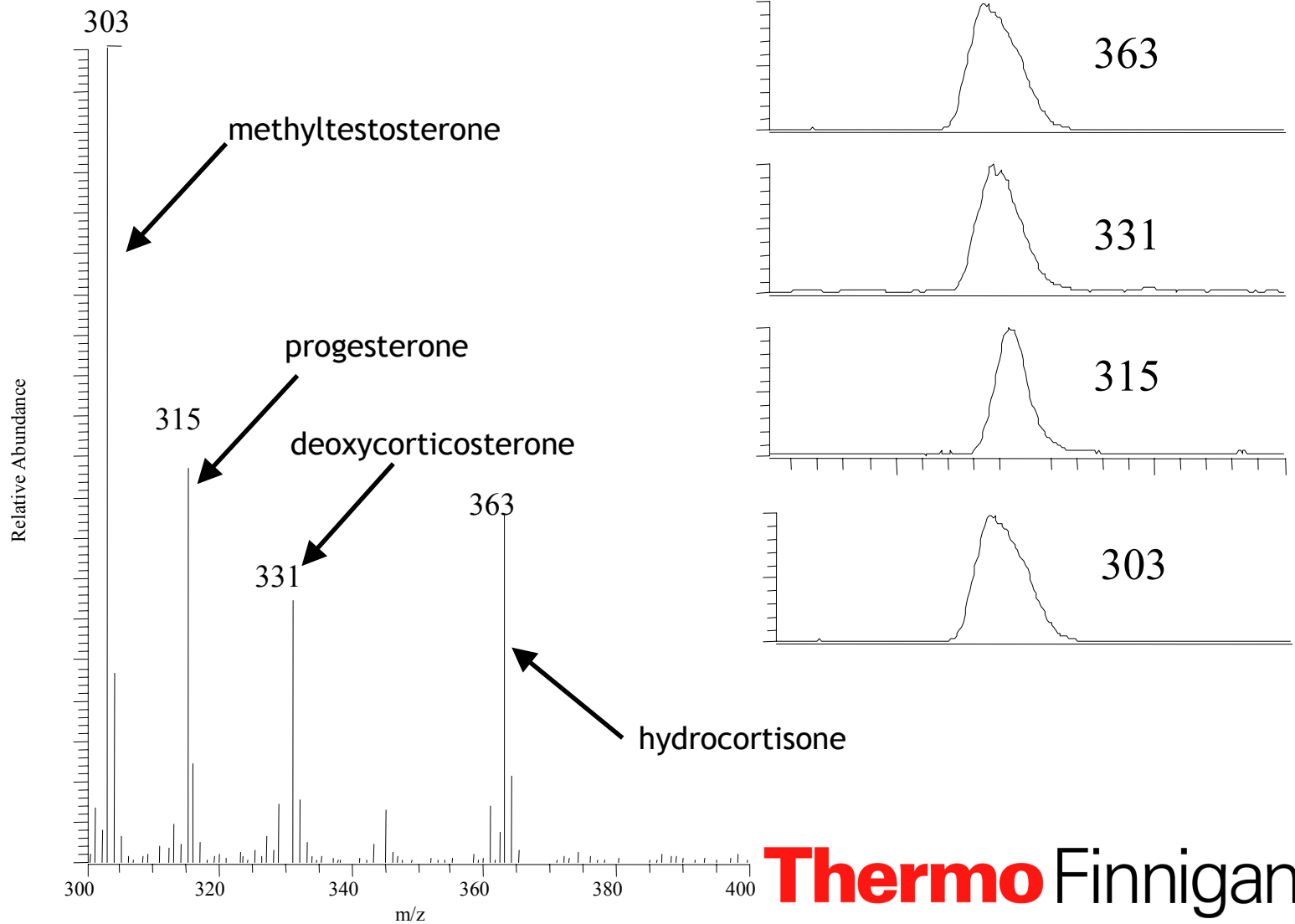
Detection by UV



Steroids coelute

No distinguishing UV spectra

Detection by MS



LC/MS shorter run times

▶ Changing from 6 to 2 min / sample means :

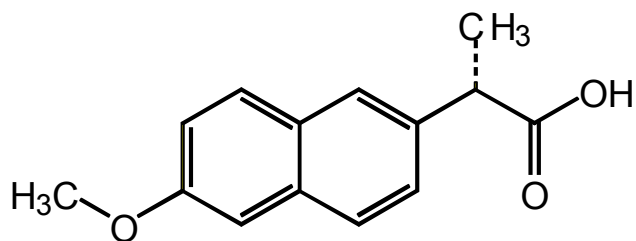
- 10 samp / hr → 30 samp / hr
- 80 samp / day → 240 samp / day
- 20,000 samp / yr → 60,000 samp / yr

Did This Horse Win The Race

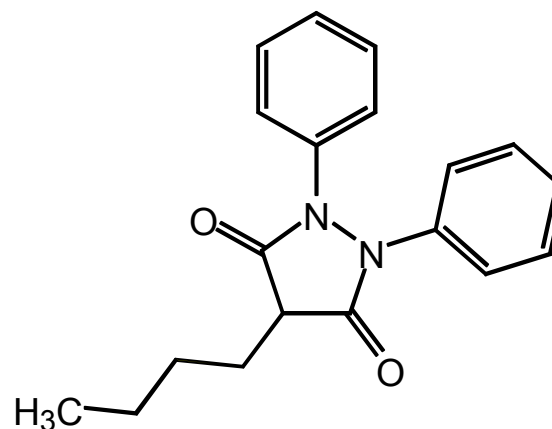
Legally ?

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

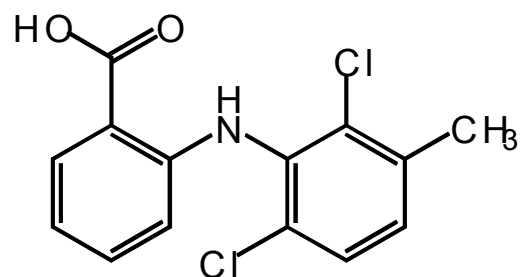
Frequently used analgesics



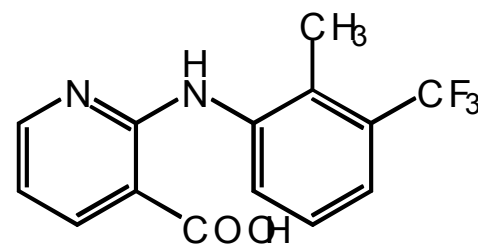
Naproxen



Phenylbutazone



Meclofenamic Acid



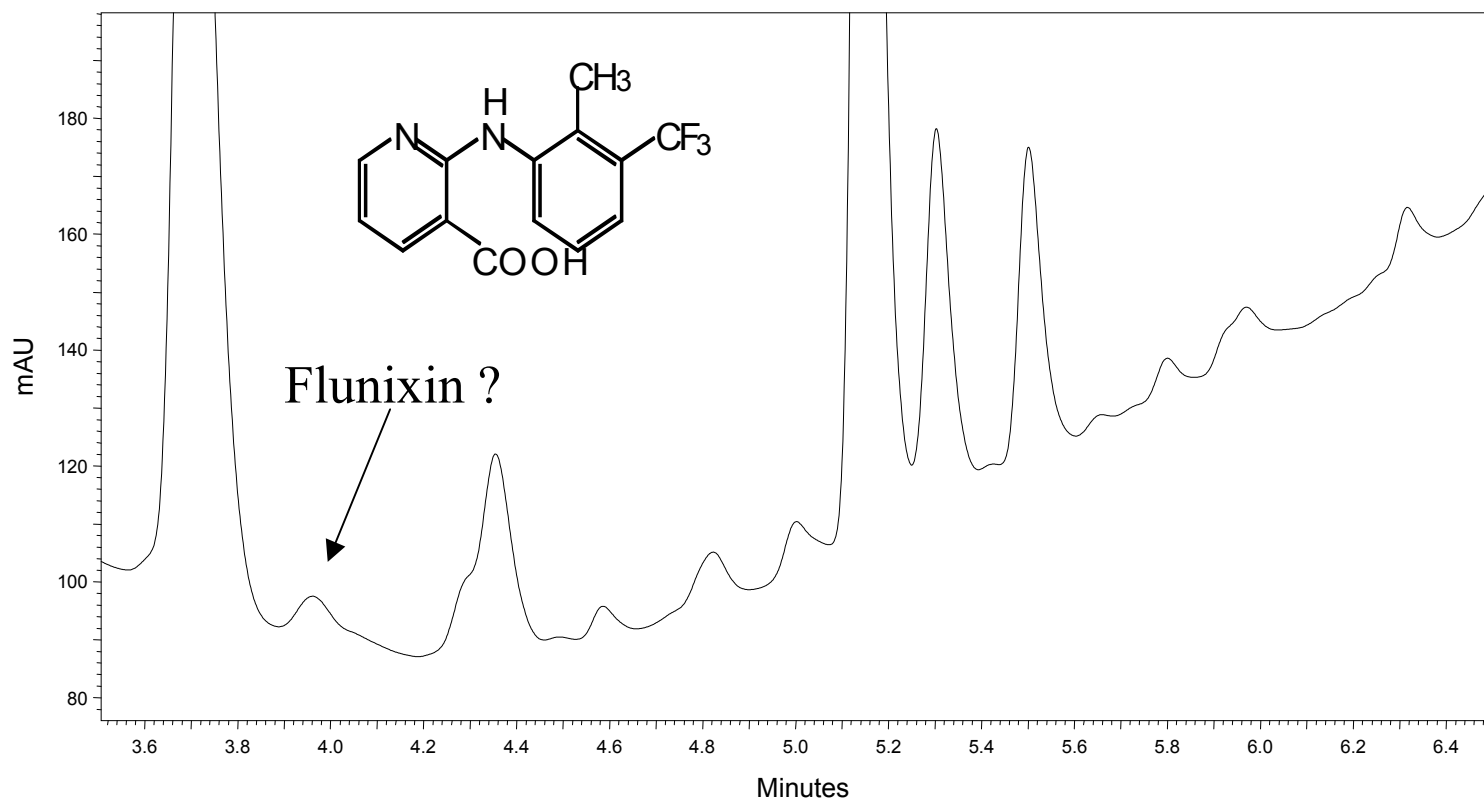
Flunixin

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Is this peak Flunixin ?

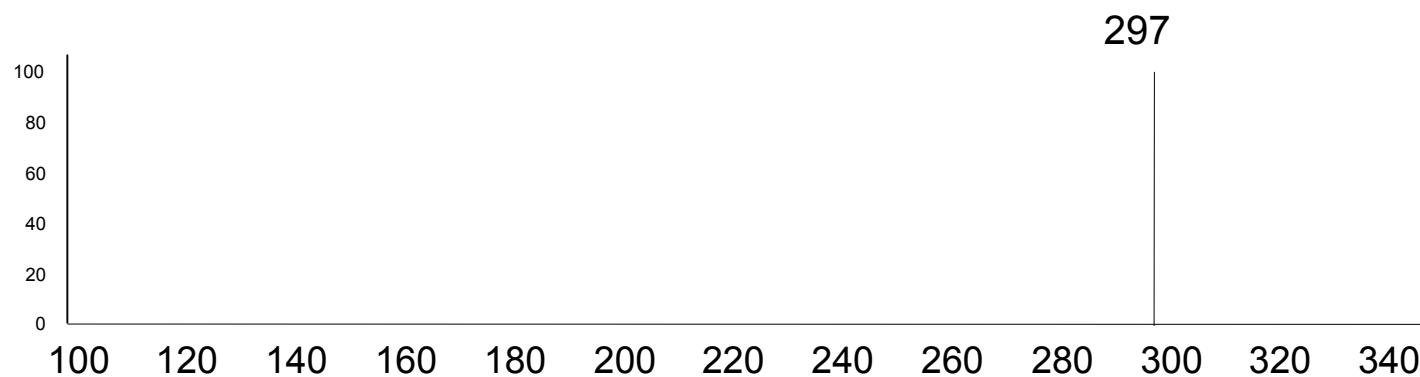
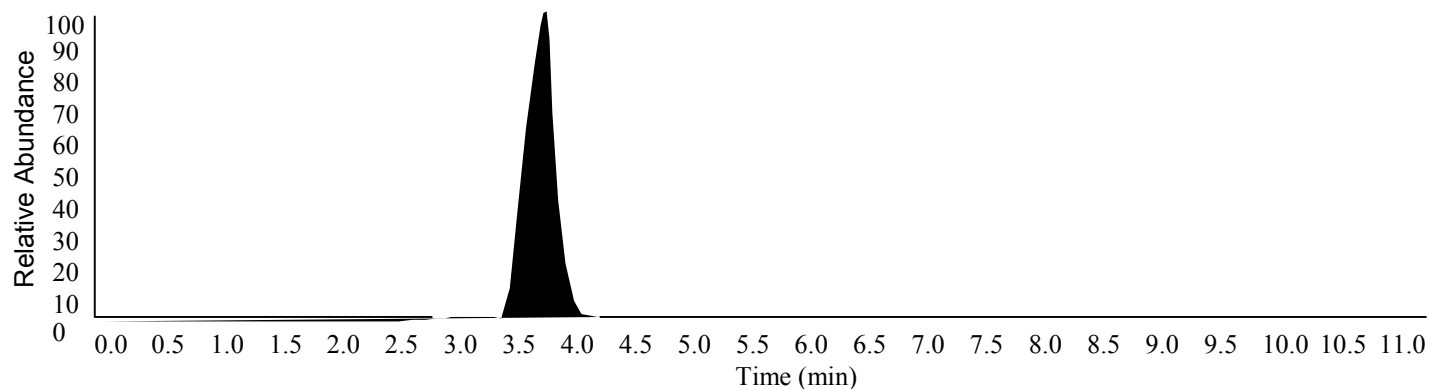
It has the correct retention time by UV

254 nm



LC/MS confirms it to be Flunixin

Flunixin Full Scan MS



m/z

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Why should I use LC/MS ?

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

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

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

LC/MS in pharmaceutical related markets

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

LC/MS in the biotechnology market

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

LC/MS in the biotechnology market

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

LC/MS in the agrochemical market

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

LC/MS in industrial markets

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

LC/MS in the environmental market

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

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

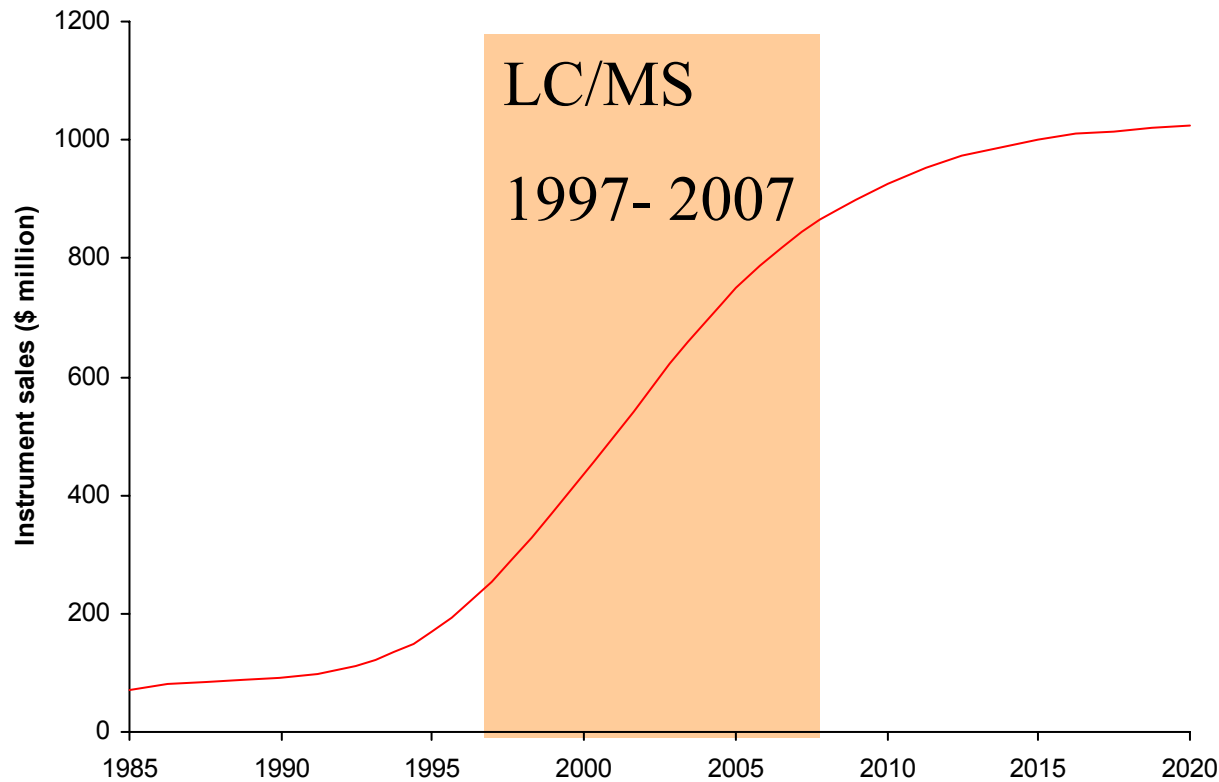
LC/MS in clinical markets

- ▶ Replace immuno assays
- ▶ Drugs of abuse

LC/MS in academia

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

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