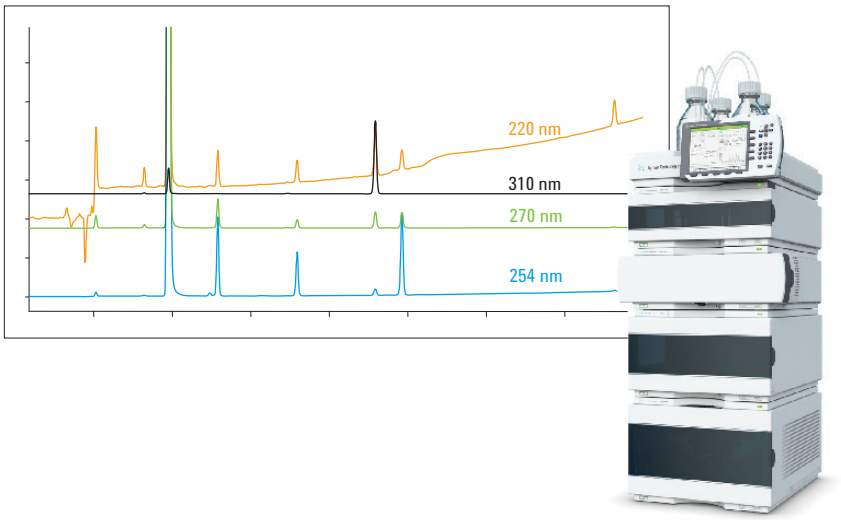
Method development on the Agilent 1290 Infinity LC using Intelligent System Emulation Technology (ISET) with subsequent transfer to an Agilent 1100 Series LC

Analysis of an analgesic drug

Technical Overview



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Abstract

Agilent's Intelligent System Emulation Technology (ISET) offers seamless transfer of methods in both directions from conventional LC systems, which have higher delay volumes and different mixing behaviors, to the Agilent 1290 Infinity LC System. A method developed on the 1290 Infinity LC System can be transferred to a different LC system by first emulating the target LC on the 1290 Infinity LC System by using ISET. This gives valid information whether the method developed on the 1290 Infinity LC System will work using the target LC system. This Technical Overview shows the development of a chromatographic method for the analysis of paracetamol and its impurities using 1290 Infinity LC System with ISET. Having developed the method it was transferred to an Agilent 1100 Series Quaternary LC System. Retention times and resolution of the different experiments were evaluated and compared with the data obtained on the 1290 Infinity LC System with ISET.

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Introduction

In the pharmaceutical industry, method development for QA/QC is done in the R&D departments. The instrumentation used in R&D is often not the same as deployed routinely in the QA/QC departments. This can lead to problems because the developed and validated method might not fulfill the requirements when transferred to a different LC system. The 1290 Infinity LC System with ISET offers the possibility to emulate the target LC and to find out whether a method will run on a different LC system without problems and delivering the same results for retention times and resolution.

This Technical Overview shows the development of a method for the analysis of paracetamol and its impurities using the 1290 Infinity LC System. Having finalized the method, the 1290 Infinity LC System with ISET emulated the target LC, an 1100 Series Quaternary LC System, to determine whether the developed method was suitable for the 1100 Series LC System. Later on, the method was transferred to the 1100 Series Quaternary LC System and the results were compared to data obtained on the 1290 Infinity LC System with ISET.

Experimental

Instrumentation and software

The Agilent 1290 Infinity LC System used for the experiments consisted of the following modules:

- Agilent 1290 Infinity Binary Pump (G4220A)
- Agilent 1290 Infinity Autosampler with Thermostat (G4226A, G1330B)
- Agilent 1290 Infinity Thermostatted Column Compartment (G1316C)
- Agilent 1260 Infinity Diode Array Detector (G4212A)

The Agilent 1100 Series LC was used for the experiments consisting of the following modules:

- Agilent 1100 Series Quaternary Pump (G1311A)
- Agilent 1100 Series Autosampler (G1313A)
- Agilent 1100 Series Thermostatted Column Compartment (G1316A)
- Agilent 1100 Series Diode Array Detector (G1315B)

Agilent ChemStation revision C.01.03 and ISET revision 1.0 were used for the experiments. All LC modules had firmware revisions A.06.32, B.06.32 or B.06.41 or higher, and all modules had RC.Net drivers.

Sample

The following mixture of compounds was used for the experiments:

Main:	Paracetamol
Impurity A:	2-Acetamidophenol
Impurity B:	N-(4-Hydroxyphenyl) propamide
Impurity F:	Nitrophenol
Impurity H:	4-(Acetylamino) phenyl Acetate (N,O-Diacetyl-4-aminophenol)
Impurity J:	4-Chloroacetanilide
Impurity K:	4-Aminophenol

Chromatographic conditions

Column:	Agilent ZORBAX SB C18, 150 × 4.6 mm, 5 µm (883975-902)
Mobile phase:	Water + 0.1% TFA, Acetonitrile + 0.09% TFA
Flow rate:	1.0 mL/min
Gradient:	5% ACN at 0 min, 90% ACN at 20 min
Stop time:	20 min
Post-time:	5 min
Injection volume:	5 µL
Column temp.:	30 °C
Detection:	220, 254, 270, 310/10 nm, Ref. 400/ 60 nm, 5 Hz, slit 4 nm

Results and discussion

Method development on the 1290 Infinity LC System

The separation was done using conventional chromatographic conditions. The column dimensions were 150 × 4.6 mm for length and internal diameter and the particle size was 5 µm. To increase the retention time of impurity K, the linear gradient started at low organic concentration. After 20 minutes, the mobile phase composition contained 90% organic to elute impurity A within a reasonable time, (Figure 1). Different wavelengths were necessary to be able to quantity all compounds at their absorbance maxima with high selectivity.

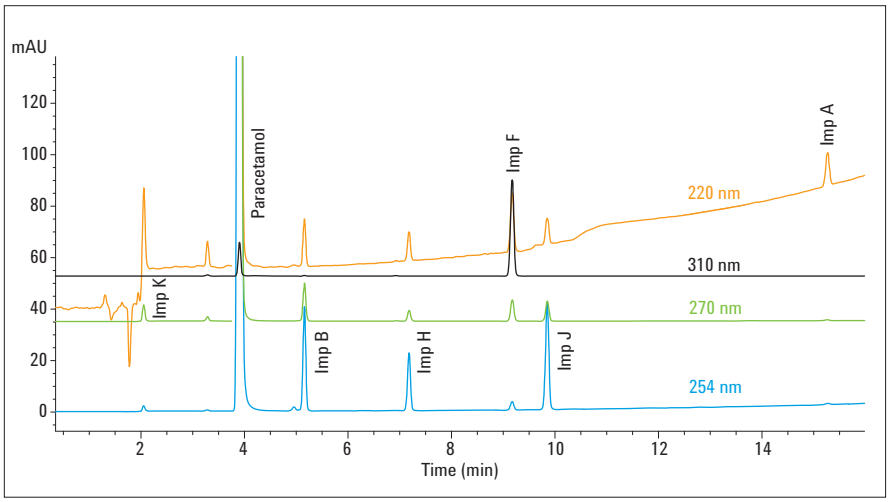

Figure 1
Overlay of chromatograms at different wavelengths.

The UV spectra, (Figure 2), delivered the information to select the optimum wavelength, (Table 1).

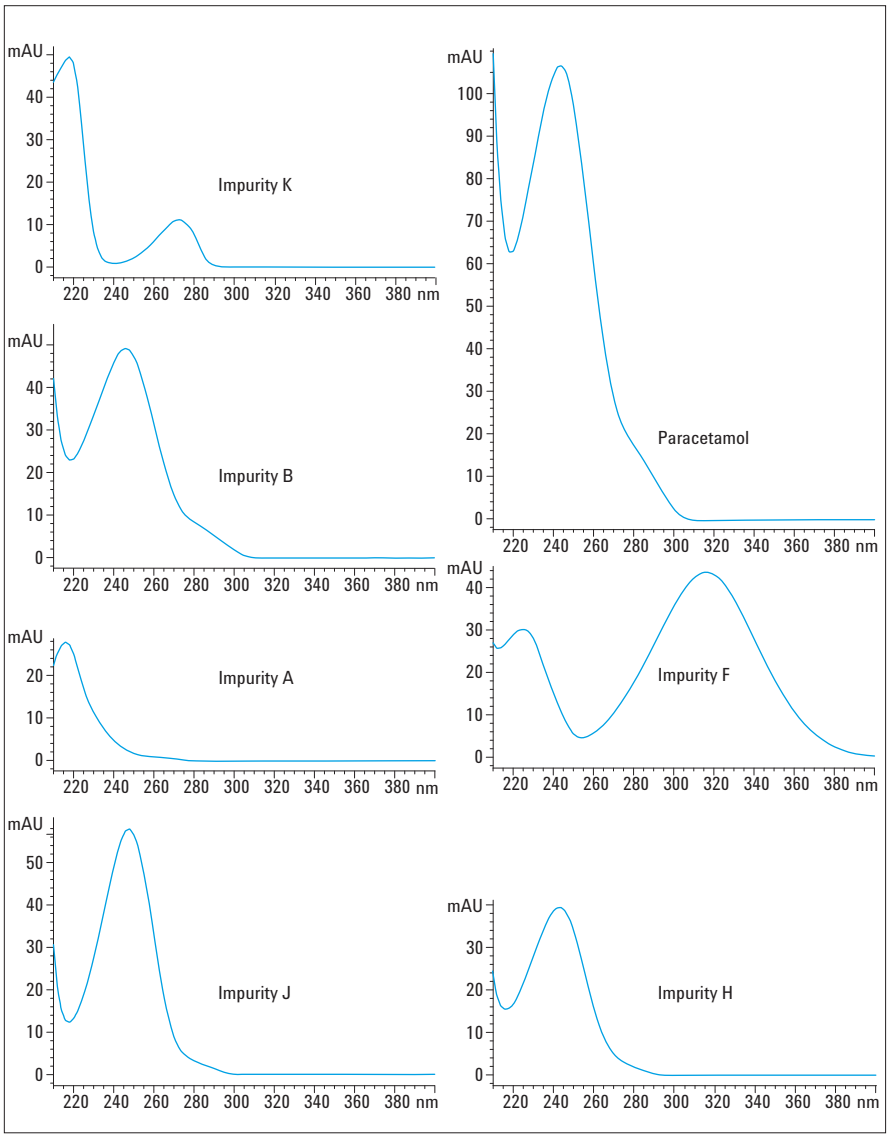

Figure 2
UV spectra of paracetamol and its impurities.

Compound	Detector wavelength
Impurity K	270 nm (better selectivity)
Paracetamol	270 nm (within linear range)
Impurity B	254 nm (absorbance maximum)
Impurity H	254 nm(absorbance maximum)
Impurity F	310 nm (absorbance maximum)
Impurity J	254 nm (absorbance maximum)
Impurity A	220 nm (absorbance maximum)

Table 1
Optimum wavelength for paracetamol and its impurities.

Emulation of the 1100 Series Quaternary LC System on the 1290 Infinity LC System using ISET and method transfer to the 1100 Series Quaternary LC System

The ISET tool on the 1290 Infinity LC System was enabled to emulate the 1100 Series Quaternary LC System. The finalized method was applied to the 1290 Infinity LC System using ISET to get an overview whether the method will work on an 1100 Series LC System. The method was then transferred to an 1100 Series Quaternary LC System. The 3 chromatograms obtained on the 1290 Infinity LC System with and without ISET and obtained on the 1100 Series quaternary LC System were compared, (Figure 3).

The retention times and the resolution using the 1290 Infinity LC System with ISET showed excellent agreement with the results of the 1100 Series Quaternary LC System. The deviation of retention times from the 1100 Series LC System data are combined in Figure 4.

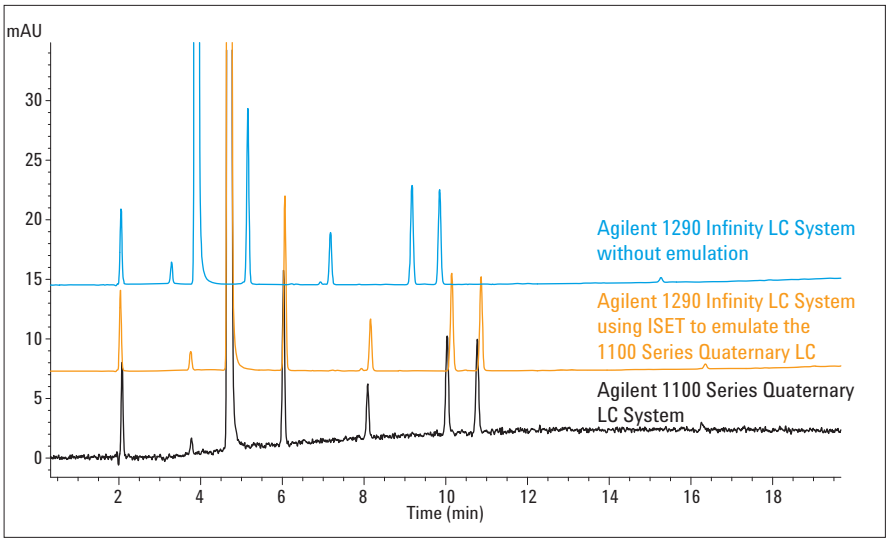

Figure 3
Overlay of chromatograms at 270 nm obtained on the Agilent 1290 Infinity LC System, on the Agilent 1290 Infinity LC System with ISET and on the Agilent 1100 Series Quaternary LC System.

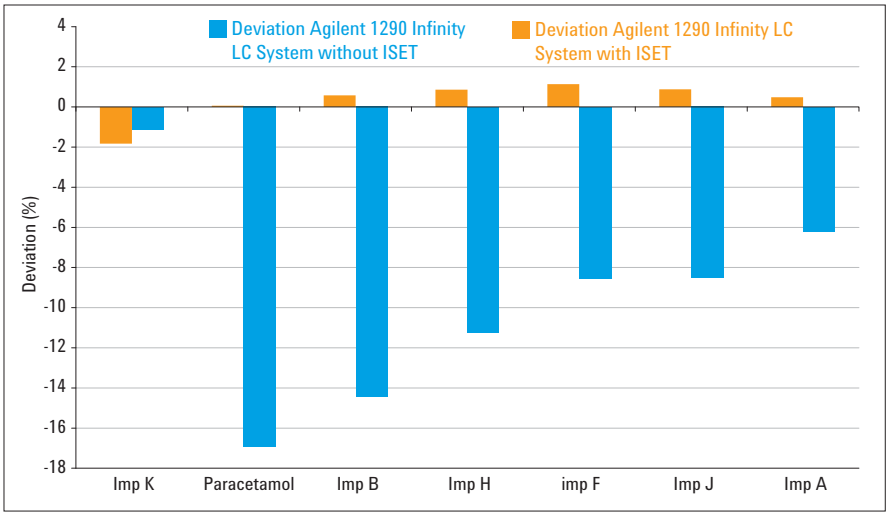

Figure 4
Deviation of retention times for the Agilent 1290 Infinity LC System with and without ISET in comparison with Agilent 1100 Series Quaternary LC System data.

The retention time deviation for the 1290 Infinity LC System with ISET was between 0.5 and 1.9%. The retention time deviation for the 1290 Infinity without ISET was as high as 17%. The results reading the resolution data are combined in Figure 5.

The deviation of the resolution on the 1290 Infinity LC System with ISET was between 0.11 and 2.4%. The deviation of the resolution on the 1290 Infinity LC System without ISET was up to 31%.

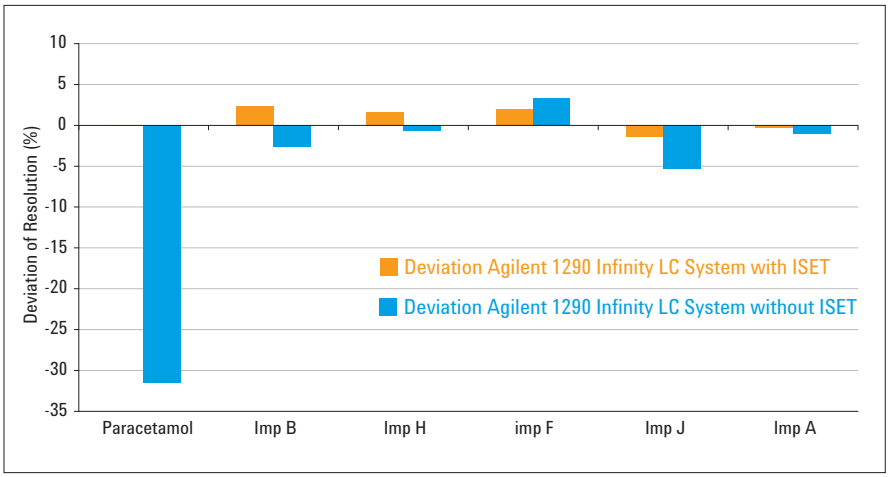

Figure 5
Deviation of resolution for the Agilent 1290 Infinity LC System with and without ISET compared with data obtained on the Agilent 1100 Series Quaternary LC System.

Conclusion

A method developed on an Agilent 1290 Infinity LC System for the analysis of paracetamol and its impurities was seamlessly transferred to an Agilent 1100 Series Quaternary LC System. To facilitate transfer the ISET function of the 1290 Infinity LC System was activated to emulate the 1100 Series LC System. This provided information whether the developed method worked on the target 1100 Series LC System. The results for retention times and resolution obtained on the 1100 Series LC System and the 1290 Infinity LC System using ISET were compared. The retention times differed less than 1.9% and the resolution less than 2.4%.

Reference

1.
"Agilent 1290 Infinity LC with Intelligent System Emulation Technology", Agilent Technologies Brochure, publication number 5990-8670EN, **2011**.

www.agilent.com/chem/iset

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