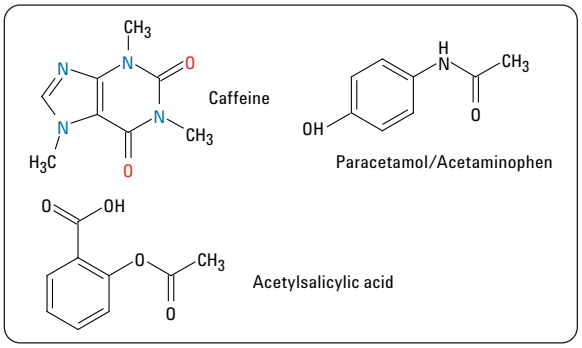
Seamless method transfer from the Agilent 1200 Series to the Agilent 1220 and 1260 Infinity LC systems

Comparison of system suitability results according to USP method USP/NF 23 for the analysis of Paracetamol (Acetaminophen) and Aspirin in pain relievers

Technical Overview



Introduction

Regulated environments in the pharmaceutical industry use validated methods that must be in compliance with EP or USP regulations. A requirement for all new instrumentation is that validated methods on the new instrument give results within the operating range and acceptance criteria of existing instruments. This eliminates the time consuming and costly need to revalidate an existing method.

The analysis of paracetamol and aspirin in pain relievers was chosen to demonstrate that seamless method transfer is possible (Figure 1). An isocratic method with UV detection was used according to USP/NF 23.

This analysis used the system suitability test, developed on an Agilent 1200 Series LC system to test whether the Agilent 1220 and Agilent 1260 Infinity LC systems fulfilled the acceptance criteria. The chromatographic conditions of the system suitability test transferred to the Agilent 1260 and Agilent 1220 Infinity LC systems without changes. The results obtained were compared for compliance with results typically obtained on the Agilent 1200 Series LC system.

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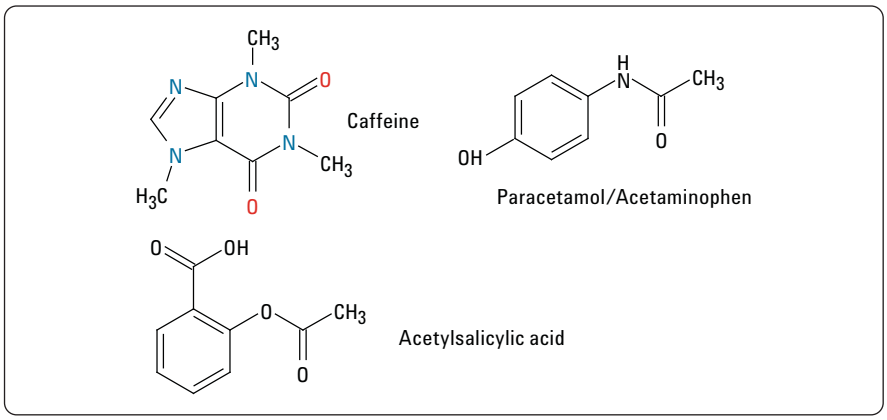

Figure 1
Structures of acetaminophen (paracetamol), aspirin and caffeine.

Experimental

Instrumentation

A standard Agilent 1200 Series LC system, an Agilent 1220 Infinity LC system and an Agilent 1260 Infinity LC system with the following configurations were used:

Configuration of the Agilent 1220 Infinity LC system (G4290B)	Configuration of the Agilent 1260 Infinity LC system	Configuration of the Agilent 1200 Series system
Gradient pump and vacuum degasser	Quaternary pump with integrated vacuum degasser (G1311B)	Quaternary pump (G1354A) with external degasser vacuum degasser (G1322A)
Column oven	Column compartment (G1316A)	Column compartment (G1316A)
Variable wavelength detector with 10 mm path length cell	Diode array detector (G4212B) with 10 mm path length cell	Diode array detector (G1315D) with 10 mm path length cell
Standard Auto sampler, sample cooling not available	Autosampler (G1367E) + sample cooling unit at 20 °C	Standard Autosampler +sample cooling unit at 20 °C
Software: ChemStation B.04.02	Software: ChemStation B.04.02	Software: ChemStation B.04.02

Table 1
Instrument configurations.

Chromatographic conditions according to USP method	
Column:	Agilent ZORBAX Eclipse Plus, 3 mm × 100 mm, 3.5 µm (internal diameter 35% less than original method, particle size 30% less than original method)
Mobile phase:	Water/methanol/acetic acid = 69/28/3
Pump settings:	No gradient (in accordance with EP regulations)
Stop time:	5 min
Flow rate:	1 mL/min, isocratic (50% less than original method)
Injection volume:	10 µL
Column temp:	45 °C
Detector:	Agilent 1220 Infinity LC system with 10 mm path length flow cell Agilent 1200 Series system with 10 mm path length Agilent 1260 Infinity LC system with 10 mm path length Peak width 0.05 min (10 Hz) Signal 275 nm

The original method was changed according to the typical allowed changes for chromatographic parameters (Table 2).

For all experiments the same column, same batch of prepared sample and the same batch of mobile phase was used.

Preparation of samples

The reference solution was prepared as follows (Table 3).

Chromatographic parameter	Typically allowed changes
Mobile phase pH	± 0.2 units
Concentration of salts in buffers	± 10%
Ratio of mobile phase percentages	± 30% of the minor component, or 0.2% absolute value of that component, whichever is greater. However, a change in any component cannot exeed ± 10% absolute, nor can the final concentration be reduced to zero.
Wavelength or UV detector	No change permitted
Column length	± 70%
Internal diameter of column	± 50%
Particle size of column packing material	Can be reduced by 50%
Flow rate	± 50%
Injection volume	Increased to as much as twice the volume specified, provided no adverse effects. Must be within stated linearity range of the method
Column compartment temperature	± 10 °C

Table 2
Typically accepted changes for USP methods.

	Stock solution in mobile phase	1: 5 diluted in water
Acetaminophen	5.5 mg/10 mL	1.1 µg/10 µL
Caffeine	1.3 mg/10 mL	0.26 µg/10 µL
Aspirin	3.9 mg/10 mL	0.78 µg/10 µL
Benzoic acid	4 mg/10 mL	0.8 µg/10 µL
Salicylic acid	4 mg/10 mL	0.8 µg/10 µL

Table 3
Sample concentration.

Results and Discussion

System suitability testing verified that the LC system fulfills the acceptance criteria typical for USP methods. The following acceptance criteria were evaluated:

- Precision of areas must be < 2% RSD
- Precision of retention times must be < 0.5% RSD
- Resolution must be > 1.4
- Tailing factor for < 1.3
- Peak symmetry > 0.75

Evaluation of column performance parameters such as symmetry and tailing factors determine the influence of different instruments on these parameters.

Figure 2 shows an overlay of the chromatograms obtained on the three Agilent LC systems.

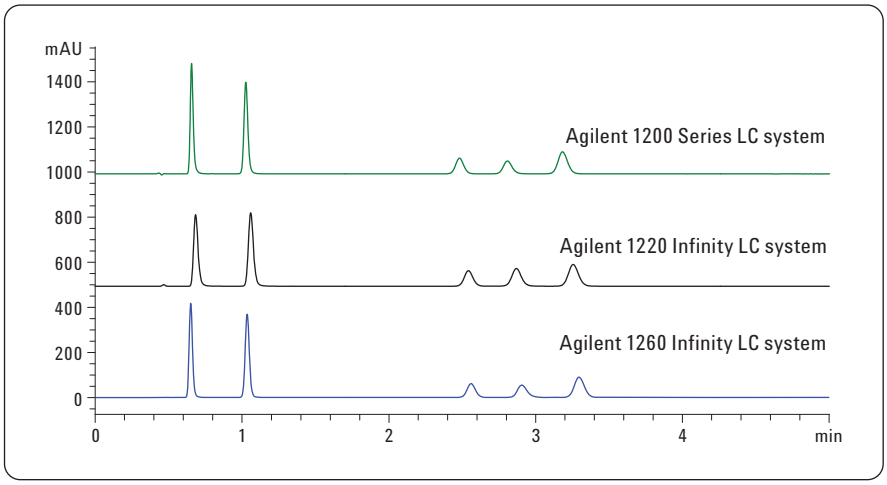

Figure 2
Overlay of chromatograms.

The difference in retention times is less than 5% from the reference chromatogram of the Agilent 1200 Series LC system. The system suitability test was applied to both new instruments and the results compared to those obtained on the Agilent 1200 Series LC system. In Tables 4–6, the results are combined. Data for retention times, symmetry, USP tailing and resolution can be obtained from the "Extended Performance" report. This report is based on calibrated peaks. Signal-to-noise data are included in the "Performance and Noise" report. Statistical data are included in the "Sequence Summary" report. All report styles are available from the "Specify Report" menu in the ChemStation.[1]

	Agilent 1200 Series LC system		Agilent 1220 Infinity LC system		Agilent 1260 Infinity LC system	
Compound	Retention time (min)	Resolution (hH)	Retention time (min)	Resolution	Retention time (min)	Resolution
Acetaminophen	0.656		0.684		0.654	
Caffeine	1.025	8.822	1.059	6.401	1.040	8.198
Aspirin	2.480	19.535	2.541	17.419	2.569	19.604
Benzoic acid	2.807	3.095	2.869	2.905	2.917	3.168
Salicylic acid	3.182	3.281	3.255	3.181	3.306	3.242

Table 4
Comparison of retention times, signal-to-noise and resolution data.

Figure 3 shows an overlay of six consecutive runs performed on the Agilent 1220 Infinity LC system for precision, evaluation of retention times and areas.

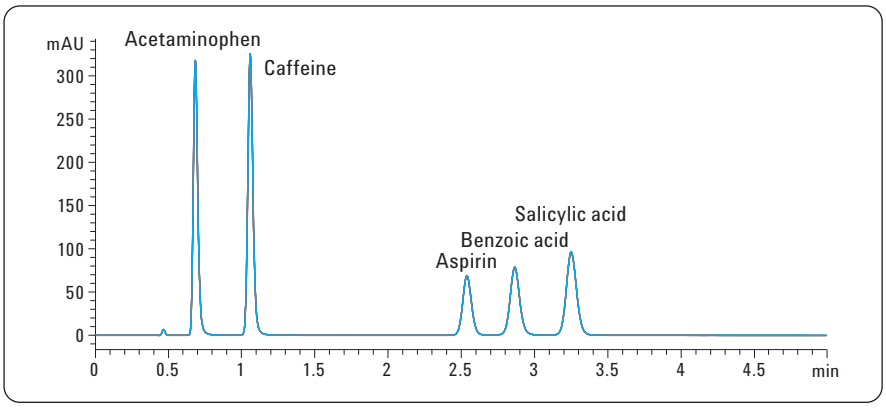

Figure 3
Overlay of six consecutive runs using the Agilent 1220 Infinity LC system; evaluation of precision data.

	Agilent 1200 Series LC System		Agilent 1220 Infinity LC System		Agilent 1260 Infinity LC System	
Compound	**RSD RT (%)**	**RSD area (%)**	**RSD RT (%)**	**RSD area (%)**	**RSD RT (%)**	**RSD area (%)**
Acetaminophen	0.107	0.1012	0.043	0.0740	0.053	0.1227
Caffeine	0.068	0.0447	0.020	0.1291	0.036	0.0323
Aspirin	0.032	0.0797	0.019	0.0959	0.020	0.1260
Benzoic acid	0.032	0.1089	0.010	0.1034	0.018	0.2026
Salicylic acid	0.024	0.0303	0.025	0.0776	0.018	0.0270

Table 5
Comparison of precision data.

	Agilent 1200 Series LC System		Agilent 1220 Infinity LC System		Agilent 1260 Infinity LC System	
Compound	**Peak symmetry**	**Peak tailing**	**Peak symmetry**	**Peak tailing**	**Peak symmetry**	**Peak tailing**
Acetaminophen	0.782	1.270	0.765	1.254	0.833	1.142
Caffeine	0.841	1.136	0.818	1.168	0.891	1.094
Aspirin	0.908	1.060	0.903	1.080	0.917	1.061
Benzoic acid	0.866	1.122	0.905	1.082	0.857	1.137
Salicylic acid	0.889	1.069	0.889	1.079	0.883	1.079

Table 6
Comparison of peak symmetry and peak tailing.

The results for the Agilent 1220 Infinity LC and the Agilent 1260 Infinity LC systems show that both systems are fully compliant with system suitability acceptance criteria stated for the Agilent 1200 Series LC system.

Conclusion

Seamless method transfer is possible for the analysis of acetaminophen (paracetamol) in pain relievers using an isocratic EP method. The system suitability test, developed on an Agilent 1200 Series LC system for this method, was applied on the new Agilent 1260 Infinity LC and the Agilent 1220 Infinity LC systems. The obtained results were compared with results typically obtained on the Agilent 1200 Series LC system (Table 6).

Both new instruments fulfilled the acceptance criteria of the system suitability test. The retention time shift for all peaks was < 5% using the same column and the same batch of mobile phase. The precision of retention times were better on the Infinity LC systems than on the original Agilent 1200 Series LC system.

Reference

1.
"Understanding Your ChemStation," Agilent Literature, G2070-91124, **2007.**

Parameter and acceptance criteria	Agilent 1200 Series LC System	Agilent 1220 Infinity LC System	Agilent 1260 Infinity LC System
RSD RT < 0.5% RSD	0.024–0.107%	0.010–0.043%	0.018–0.053 %
RSD area < 2% RSD	< 0.11%	< 0.13%	< 0.21%
Rs > 1.4 Benzoic acid	3.095	2.869	3.168
Tailing factors < 1.3	< 1.28	< 1.26	< 1.15
Symmetry factors > 0.75	> 0.78	> 0.766	> 0.853

Table 6
Comparision of acceptance criteria.

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