Application Note

Pharma & Biopharma

Analysis of Zolmitriptan and Related Compounds Using the Agilent 7100 Capillary Electrophoresis System

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Abstract

This Application Note describes the analysis of zolmitriptan and its impurities using the Agilent 7100 Capillary Electrophoresis (CE) system. The zolmitriptan United States Pharmacopeia (USP) method was replicated using the 7100 CE system. The samples used for the analysis were standards involving zolmitriptan and related compounds. After performing the analysis, resolution and RSD values were compared to that of the USP method.

Introduction

CE offers fast separations with exceptional efficiency and resolution for analytical challenges that often can only be met with difficulty by LC. In addition, CE offers the advantage that several separation modes can be run on a single instrument. This makes CE a very versatile technique for a broad range of applications and separation challenges. This Application Note describes the analysis of zolmitriptan API along with impurities using the 7100 CE system.

Experimental

Instrumentation

The analysis was performed using the 7100 CE system.

Software

Agilent OpenLab CDS ChemStation Rev. C.01.07 [27]

Parameters

Method parameters, such as buffers, sample preparations, and so forth were established according to the USP method. Table 1 details these method parameters.

Materials

- **Samples:** Zolmitriptan RS, related compound F, related compound G, and R-isomer standards
- **Internal standard:** Tryptamine hydrochloride
- **Chemicals:** Sodium borate decahydrate and hydroxypropyl cyclodextrin were procured from Sigma-Aldrich

Sample preparation as per the USP

- **Internal standard:** 0.2 mg/mL of tryptamine hydrochloride in diluent
- **System suitability testing:** 0.01 mg/mL of tryptamine hydrochloride from internal standard solution, 1 mg/mL of zolmitriptan standard, and 0.01 mg/mL of related compound G, related compound F, and R-isomer
- **Standard solution:** 0.01 mg/mL of tryptamine hydrochloride from internal standard solution and 0.001 mg/mL of zolmitriptan standard in diluent

Table 1. Method parameters used in analysis.

Parameters	Value
Buffer used	19.1 g/L Sodium borate decahydrate in water. pH adjusted with phosphoric acid to 2.1
Run buffer	50 mg/mL Hydroxypropyl cyclodextrin in buffer
Diluent	0.02 M Hydrochloric acid
Voltage	20 kV
Detection	UV, 200 nm
Injection	50 mbar for 5 seconds
Capillary temperature	25 °C
Capillary used	Agilent uncoated fused silica 75 µm × 56 cm
Conditioning for new column	**Inlet:** Capillary was flushed with 1 N NaOH for 10 minutes, 5 minutes with 0.1 N NaOH, and 5 minutes with water from inlet **Outlet:** Collect all the flushes in Milli-Q water at the outlet
Preconditioning	**Inlet:** Capillary was flushed with water for 1 minute, 1 minute with 0.1 N NaOH, 1 mL with water, and 4 minutes with running buffer from inlet **Outlet:** Collect all the flushes in Milli-Q water at the outlet

Results and Discussion

This study replicates the zolmitriptan USP method using the 7100 CE system. However, there was a slight difference in the capillary length compared to that specified in the pharmacopeia. The capillary length mentioned in the USP was 50 cm, whereas we used a capillary of 56 cm in length. As per the USP method, the voltage mentioned was 15 kV. However, because of the slight deviation in the capillary length, a difference in the selectivity of one of the impurity peaks (related compound F) was observed with 15 kV. Zolmitriptan related compound F was found to elute late with a 15 kV voltage (data not shown).

Therefore, to obtain the best result, a small amount of method development was performed using different voltage conditions. Voltages from 15 to 22 kV were tested. The best voltage for the separation of zolmitriptan and all the impurities was 20 kV. With this optimized voltage, system suitability trials, standard analysis, and so forth were performed. Figures 1 and 2 show the electropherograms for the standard and system suitability analyses, respectively.

From the system suitability solution, the resolution and the relative migration time of the peaks were calculated. All the peaks were found to have a resolution >1.5, mentioned as a criterion in the USP method. The resolution of all the peaks were tabulated and are shown in Table 2. A comparison of the relative migration time obtained in the experiments with that of the USP values is tabulated in Table 3. Replicate injections of the standard solutions were performed, and the %RSD values were calculated (Figure 3).

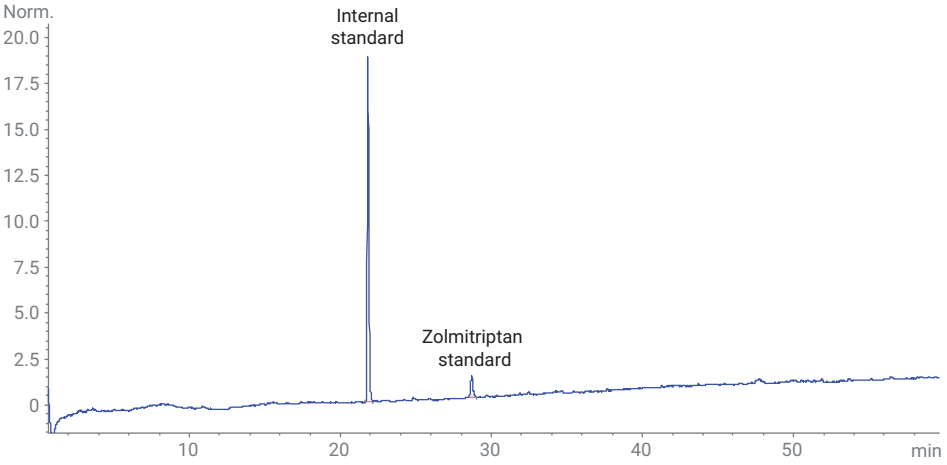

Figure 1. Electropherogram for the standard analysis.

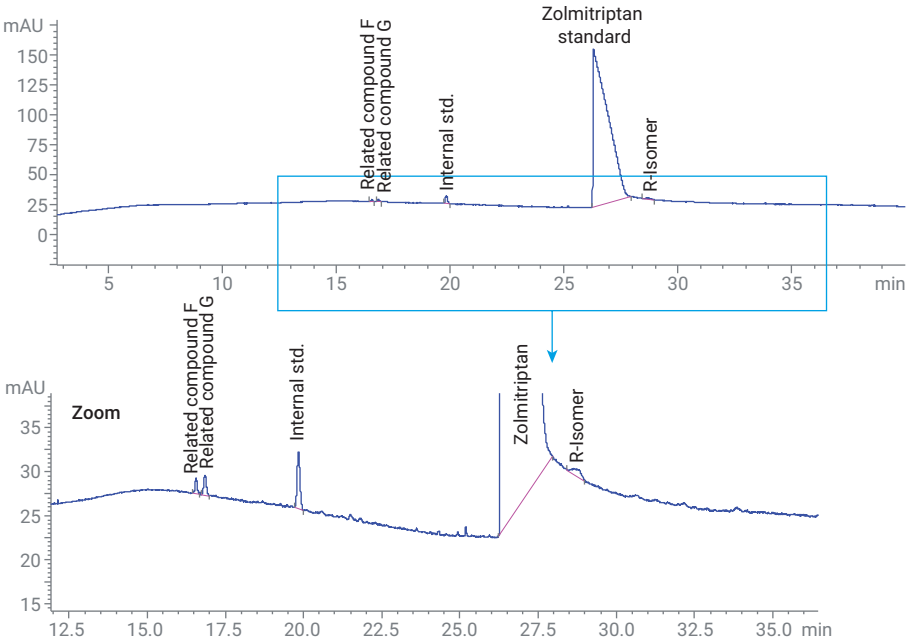

Figure 2. The electropherogram of the system suitability solution along with a zoomed view. All the peaks were found to have a resolution greater than 1.5, mentioned as an acceptance criterion in the USP method.

Table 2. Resolution details of the peaks from the system suitability solution.

Peak	Tangent resolution
Relative compound G	2.18
Internal standard	18.01
Zolmitriptan standard	24.76
R-isomer	7.74

As per the pharmacopeia method, the RSD values should not be more than 5 %. After the replicate injections, the RSDs were found to be 2.4 %, which is within the limits of the USP specifications.

Conclusion

CE is an orthogonal technique to LC. In CE, the preparation of samples and solvents is minimal, and it can be considered a green technology. Using the 7100 CE and related capillaries, we successfully analyzed zolmitriptan and related compounds as per the USP method. After analysis, the results obtained were found to be comparable to that of the limits dictated in the USP method.

Table 3. Comparison of relative migration time of the peaks between the USP and the observed experimental values.

Peaks	USP value	Experimental value
API (zolmitriptan)	1	1
Relative compound F	0.68	0.63
Relative compound G	0.71	0.66
Internal standard	0.78	0.75
R-isomer	1.07	1.1

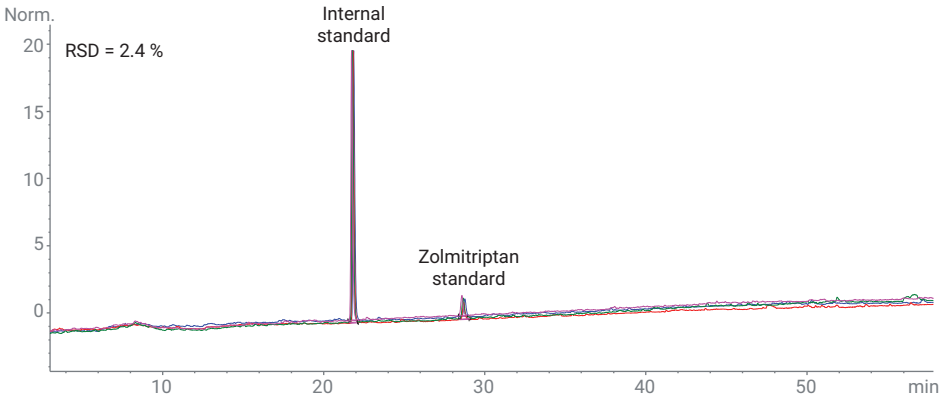

Figure 3. Overlay of replicates of standard solution.

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