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Extraction and LC–MS-MS Analysis of Desloratadine and 3-Hydroxy Desloratadine from Human Plasma with SPEC® SCX

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This application describes the use of SPEC® SCX monolithic SPE sorbent and reverse-phase HPLC for the isolation of desloratadine and 3-hydroxy desloratadine from plasma. Analysis was completed via triple-quadrupole MS monitoring MRM transitions using electrospray ionization (ESI).

Desloratadine (Clarinex®) is a long-acting tricyclic histamine antagonist with selective H1-receptor histamine antagonist activity. It is an active metabolite of loratadine (Claritin®) that is further metabolized to 3-hydroxydesloratadine, another active metabolite. Both desloratadine and 3-hydroxydesloratadine are therapeutically active at 1–10 ng/mL [plasma] levels. Loratadine and desloratadine are widely prescribed (estimated sales exceed $3 billion) to treat hay fever and general symptoms of allergic rhinitis (affecting 10–30% of the adult population), thus a reliable method to extract these compounds will find widespread application.

Experimental Conditions

Materials

Desloratadine: purity 98.3%
3-Hydroxy desloratadine: purity 99.3%
Human plasma with EDTA anticoagulant

SPE

The 15 mg SPEC SCX solid-phase extraction plate (Varian part number A59604) is preconditioned with 400 µL of methanol followed by 400 µL of 2% formic acid. A 250-µL sample aliquot diluted in 500 µL of 2% formic acid solution is applied to the preconditioned solid phase extraction plate under vacuum (< 5 in. Hg negative pressure). The extraction plate is washed sequentially with 400 µL of 2% formic acid solution followed by 400 µL of 2% formic acid in acetonitrile:methanol (70:30, v:v%). Analyte is eluted by using 2 × 200 µL aliquots of 4% ammonium hydroxide in methanol:acetonitrile:water (45:45:10:v:v:v%). The eluent is dried under nitrogen and reconstituted in 150 µL of mobile phase for subsequent LC–MS-MS analysis.

HPLC

Column: 2 × 50 mm C18
Conditions: 250 µL/min, gradient elution 20–90% mobile phase A (10 mM ammonium formate in methanol with 0.2% formic acid) over 3.5 min, mobile phase B = 10 mM ammonium formate in water with 0.2% formic acid.

Mass Spectrometry

A Sciex API 3000 LC–MS-MS equipped with a TurboIonspray™ interface was operated in the multiple reaction monitoring (MRM) mode using positive ion electrospray. Desloratadine is monitored with an MRM transition of *m/z* 311.2 → *m/z* 259.1 while 3-hydroxy desloratadine is monitored with an MRM transition of *m/z* 327.2 → *m/z* 275.1.

Results

Performing replicate extractions on plasma standards containing 1 to 10 ng/mL each of desloratadine and 3-hydroxydesloratadine, analysts can expect ±85% extraction efficiency relative to a spiked plasma standard. A typical chromatogram is shown in Figure 1.

Conclusion

With single-mode ion exchange SPE a highly effective isolation of desloratadine and its metabolite is quickly and easily accomplished. Optimization steps can be employed to enhance recovery, utilize the method for similar analytes, and/or minimize extraction times, e.g. using the monolithic sorbent's low dead volume feature to eliminate the drying step by eluting (quantitatively) in 2 × 75 µL.

Acknowledgment

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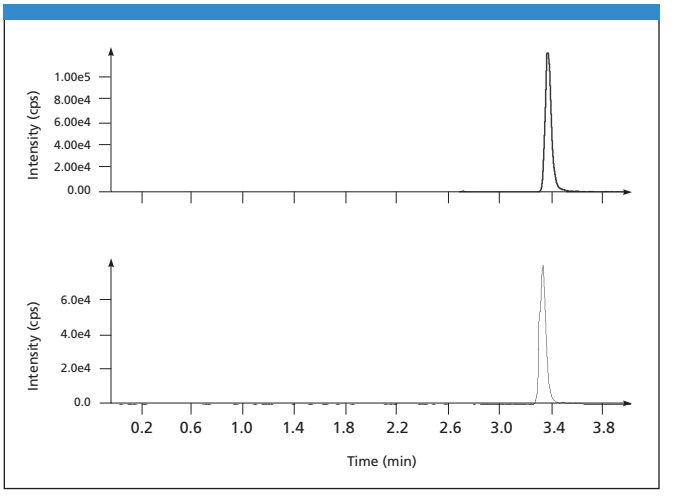

Figure 1: The upper chromatogram shows the signal for desloratadine, the lower is 3-hydroxydesloratadine.

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