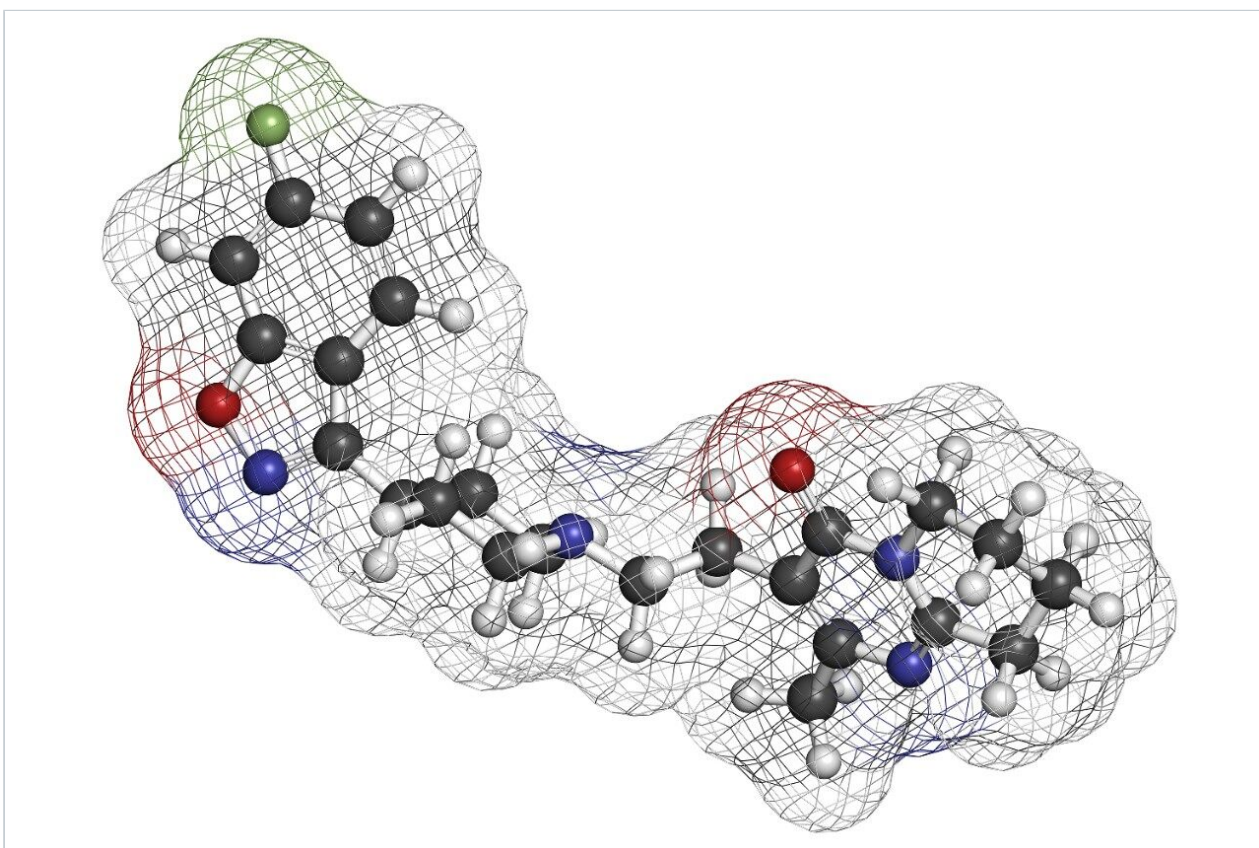


Risperidone and 9-Hydroxyrisperidone on Oasis MCX

Waters Corporation



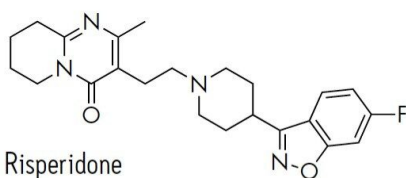
This is an Application Brief and does not contain a detailed Experimental section.

Abstract

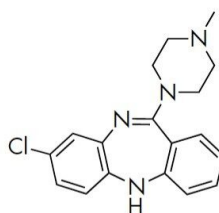
This application brief highlights the separation of risperidone and 9-hydroxyrisperidone on Oasis MCX.

Introduction

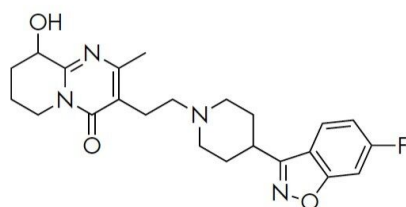
Risperidone is an antipsychotic drug and is rapidly metabolized to the 9-hydroxyrisperidone metabolite in the liver. This metabolite is the predominant circulating species with same activity as the parent and therefore, must be quantitated. All analytes are bases and therefore an Oasis MCX plate was selected.



Risperidone
M.W. 410.5
pKa = 8.24



Clozapine, ISTD
M.W. 326.8
pKa₁ = 3.7
pKa₂ = 7.6



9-Hydroxyrisperidone
M.W. 426.5

Experimental

Test Conditions

Oasis MCX 10-mg plate (P/N 186000259)

| | |
|--------------|----------------------------------------------------------------------------------------------------------------|
| Condition: | 500 μ L MeOH |
| Equilibrate: | 500 μ L H ₂ O |
| Load: | 500 μ L (250 μ L human plasma, diluted 1:1 with 4% H ₃ PO ₄ in H ₂ O) |

Oasis MCX 10-mg plate (P/N 186000259)

| | |
|---------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|
| Wash 1: | 500 µL 2% FA |
| Wash 2: | 500 µL MeOH |
| Elute: | 250 µL (125 µL x 2) 5% NH ₄ OH in MeOH |
| Options: | <ol style="list-style-type: none">1. Dilute 250 µL H₂O with 2% FA2. Evaporate/ Reconstitute3. Direct inject |
| Inject: | 10 µL |
| Column: | ACQUITY UPLC BEH C ₁₈ 2.1 x 50 mm, 1.7 µm |
| Mobile Phase A: | 0.1% HCOOH in H ₂ O |
| Mobile Phase B: | 0.1% HCOOH in MeOH |
| Flow Rate: | 0.3 mL /min |
| Injection Volume: | 10.0 µ L |
| Column Temperature: | 40 °C |
| Sample Temperature: | 10 °C |
| Instrument: | ACQUITY UPLC with Quattro Premier |

Gradient:

| Time (min) | Profile |
|------------|---------|
| | %A |
| 0.0 | 60 |

| Time (min) | Profile |
|------------|---------|
| 1.0 | 60 |
| 1.5 | 0 |
| 3.5 | 0 |
| 4.0 | 60 |
| 4.5 | 60 |

Quattro Premier

ESI+

Capillary: 3.5 kV

Source Temp.: 120 °C

Desolvation Temp.: 350 °C

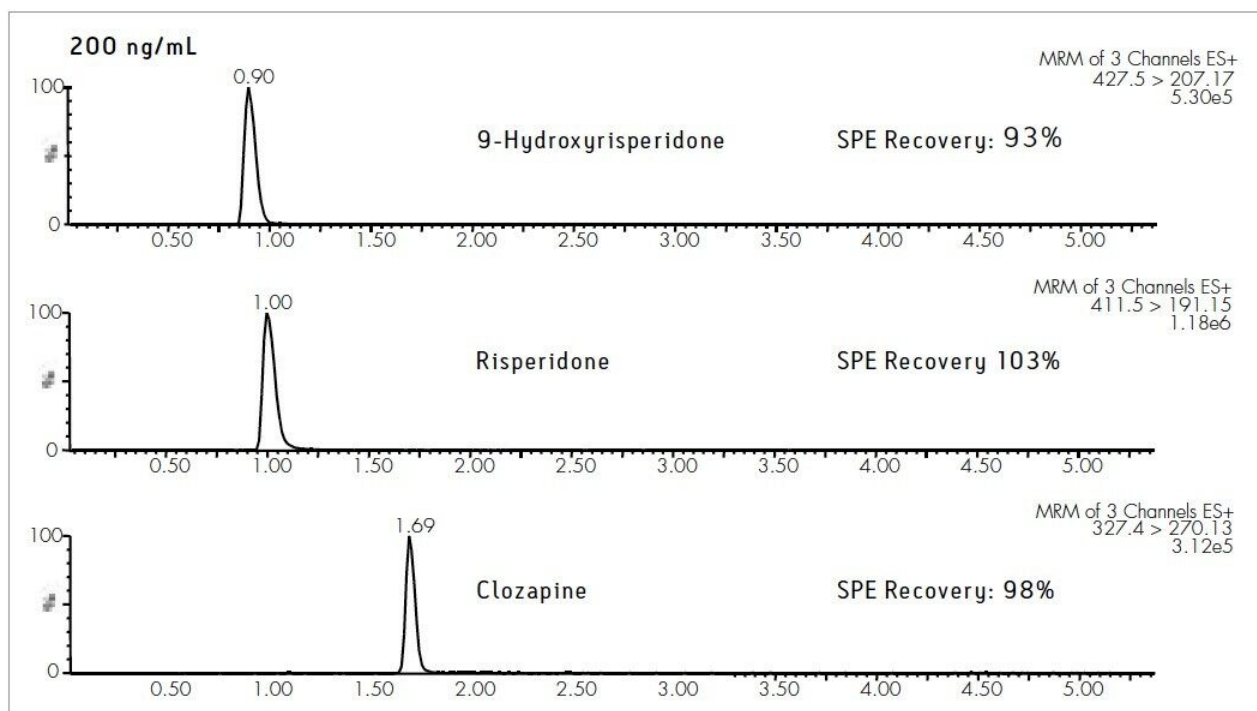
Cone Gas Flow: 0 L /Hr

Desolvation Gas Flow: 700 L /Hr

Collision Cell Pressure: 2.59 e⁻³ mbar

| Compound | Precursor Ion m/z | Product Ion m/z | Cone Voltage (V) | Collision Energy (eV) |
|--------------------------|----------------------|--------------------|---------------------|--------------------------|
| Risperidone | 411.5 | 191 | 40 | 30 |
| 9-Hydroxy risperidone | 427.5 | 207 | 40 | 30 |
| Clozapine | 327.4 | 270 | 35 | 25 |

Results and Discussion



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ACQUITY UPLC System <<https://www.waters.com/514207>>

WA60088, June 2007