Supplemental tables for

# **A robust, rapid and easy-to-use HPLC-MS/MS method for simultaneous determination** **of four antibiotics in human plasma and its application to therapeutic** **drug monitoring**

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**Supplemental Table S1**. Mass spectrometry operating parameters

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Analytes  and IS | Q1(*m/z*) | Q3(*m/z*) | DP(V) | CE(V) | RT(min) |
| linezolid | 338.2 | 296.3 | 65 | 21 | 2.87 |
| voriconazole | 350.2 | 127.1 | 65 | 40 | 3.12 |
| cefoperazone | 646.2 | 143.0 | 38 | 45 | 2.73 |
| fluconazole | 307.2 | 220.1 | 60 | 22 | 2.84 |
| linezolid-d3 | 341.2 | 297.1 | 65 | 22 | 2.85 |
| voriconazole-d3 | 353.1 | 127.2 | 65 | 32 | 3.10 |
| fluconazole-d4 | 311.3 | 223.1 | 80 | 17 | 2.83 |

**Supplemental Table S2.** Stability of linezolid, voriconazole, cefoperazone and fluconazole under tested conditions (n =6)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Analyte | Nominal  Concentration  (μg/mL) | 24 h post-preparative stability in the autosampler | | Freeze-thaw for 3 cycles at -70℃ | | 24 hours in plasma at room temperature | | 5 days in plasma  at 4°C | | 90 days in plasma at -70℃ | | 24 hours in whole blood at room temperature | | 5 days in whole blood at 4°C | |
| Accuracy  (%) | Precision (CV%) | Accuracy  (%) | Precision (CV%) | Accuracy  (%) | Precision (CV%) | Accuracy  (%) | Precision (CV%) | Accuracy  (%) | Precision (CV%) | Bias\* (%) | Precision\*\* (CV%) | Bias\* (%) | Precision\*\*  (CV%) |
| linezolid | 0.30 | 103.33 | 6.45 | 106.67 | 6.25 | 103.33 | 3.23 | 100.00 | 6.67 | 100.00 | 5.70 | 104.33 | 2.56 | 108.41 | 5.88 |
| 3.00 | 101.00 | 2.31 | 101.00 | 2.64 | 101.00 | 1.98 | 105.33 | 2.22 | 99.67 | 2.11 | 95.32 | 1.32 | 104.71 | 6.37 |
| 24.00 | 93.00 | 2.42 | 92.00 | 2.45 | 93.12 | 1.70 | 93.54 | 2.23 | 93.62 | 3.24 | 94.52 | 1.01 | 98.36 | 1.78 |
| voriconazole | 0.15 | 106.67 | 12.50 | 106.67 | 12.50 | 106.67 | 6.25 | 100.00 | 6.67 | 100.00 | 8.87 | 107.49 | 3.96 | 104.59 | 6.95 |
| 1.50 | 102.00 | 3.27 | 100.00 | 4.67 | 102.00 | 2.61 | 101.33 | 1.97 | 98.67 | 2.16 | 91.70 | 2.27 | 104.84 | 5.25 |
| 12.00 | 101.83 | 3.68 | 101.25 | 1.56 | 99.33 | 1.34 | 102.25 | 3.18 | 100.83 | 3.31 | 93.44 | 1.80 | 97.55 | 2.77 |
| cefoperazone | 1.20 | 98.33 | 5.93 | 96.67 | 10.34 | 96.67 | 3.45 | 96.67 | 9.48 | 92.50 | 3.64 | 105.06 | 12.38 | 110.11 | 9.79 |
| 12.00 | 93.33 | 2.50 | 95.25 | 4.64 | 95.67 | 2.79 | 98.75 | 3.63 | 94.58 | 1.91 | 94.64 | 2.31 | 99.88 | 8.66 |
| 96.00 | 104.14 | 3.11 | 102.94 | 2.87 | 102.00 | 1.43 | 104.92 | 3.35 | 105.07 | 2.71 | 95.86 | 0.41 | 98.29 | 2.01 |
| fluconazole | 0.30 | 103.33 | 9.68 | 106.67 | 9.38 | 100.00 | 6.67 | 100.00 | 3.33 | 103.33 | 8.32 | 99.54 | 4.67 | 104.51 | 6.43 |
| 3.00 | 99.67 | 3.68 | 102.67 | 4.22 | 100.00 | 2.33 | 105.00 | 3.17 | 101.00 | 2.48 | 95.20 | 1.02 | 101.76 | 5.50 |
| 24.00 | 92.50 | 3.20 | 93.12 | 2.55 | 92.00 | 3.22 | 96.25 | 1.65 | 94.71 | 2.71 | 93.40 | 1.91 | 97.32 | 2.82 |

\* The percentage of the average peak area of the stable samples to the average peak area of freshly prepared drug-containing whole blood samples

\*\*Peak area precision