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Supplementary Information

Optimization of an Electrolyte System for the Simultaneous Separation of Nelfinavir Mesylate and Two Impurities by Micellar Electrokinetic Chromatography

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Methods

General

NMR spectra were recorded using a Bruker DRX 400 spectrometer (^{1}H at 400 MHz and ^{13}C at 100 MHz) in DMSO-d_6 or in $CDCl_3$ or in D_2O with tetramethylsilane (TMS) as the internal standard. The low resolution mass spectrometry analyses were performed on an LC/MS micromass ZMD, using electrospray ionization in positive or negative ion mode. Samples were introduced by the standard direct insertion probe method.

Nelfinavir was synthesized from D-tartaric acid as previously described in article.

All synthesized compounds exhibited satisfactory ^{1}H NMR and mass spectra. The data spectral observed for the nelfinavir mesylate and the two main impurities arising from its synthetic route are listed below.

3-hydroxy-2-methylbenzoic acid (impurity A)

(Available from Xiamen Mchem Laboratóries Ltda) ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.95 (d, 1H, *J* 10 Hz), 7.49 (d, 1H, *J* 10 Hz), 7.24 (t, 1H, *J* 10 Hz), 2.34 (s, 3H), 2.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 169.4, 149.8, 136.5, 132.4, 130.2, 125.8, 122.1, 20.8, 16.2; LC/MS $[M - H]^-$ 150.9.

((2*R*,3*R*)-4-((3*S*,4a*S*,8a*S*)-3-(*tert*-butylcarbamoyl) octahydroisoquinolin-2(1H)-yl)-3-hydroxy-1-(phenylthio) butan-2-aminium benzoate (impurity B)

^{1}H NMR (DMSO-d_6, 400 MHz) δ 7.95 (d, *J* 10 Hz, 2H), 7.53 (d, *J* 10 Hz, 2H), 7.42-7.24 (m, 6H), 3.77-3.70 (m, 2H), 3.10-3.05 (m, 1H), 2.97-2.89 (m, 2H), 2.72 (dd, *J* 15 Hz, ^2J 5 Hz, 1H), 2.48 (t, *J* 15 Hz, 1H), 2.34 (dd, *J* 15 Hz, ^2J 5 Hz, 1H), 2.23 (dd, *J* 13 Hz, ^2J 5 Hz, 1H), 2.00 (q, *J* 15 Hz, 1H), 1.82-1.19 (m, 11H), 1.28 (s, 9H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 175.8, 175.1, 138.7, 135.2, 132.1, 131.6, 130.5, 130.4, 128.9, 128.4, 70.3, 66.9, 63.0, 60.3, 57.5, 52.3, 37.7, 35.5, 34.8, 32.2, 31.4, 29.0, 27.7, 27.1, 21.6; LC/MS $[M]^+$ 434.2.

Nelfinavir mesylate

m.p. 208 °C; optical rotation −105° to −115°; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.19 (s, 9H), 1.40-1.23 (m, 3H), 1.56-1.45 (m, 2H), 1.74-1.60 (m, 4H), 1.97-1.81 (m, 5H), 2.12 (s, 3H), 2.27 (s, 3H), 3.59-2.88 (m, 4H), 4.08-3.78 (m, 4H), 5.80-5.70 (m, 1H), 6.80 (m, 2H), 7.00-6.94 (m, 1H), 7.19-7.14 (m, 1H), 7.33-7.25 (m, 4H), 8.10 (s, 2H), 9.18-9.02 (br, 1H); ^{13}C NMR (D_2O, 100 MHz) δ 12.8, 24.1, 26.5, 27.6, 28.0, 28.1, 28.8, 33.8, 35.9, 37.5, 51.0, 52.5, 56.7, 59.4, 69.0, 72.3, 118.8, 119.6, 123.6, 124.8, 127.0, 127.4, 131.0, 134.8, 136.4, 155.6, 164.7, 172.7; IR (KBr) ν_{max}/cm^{-1} 3277, 3078, 2932, 2862, 2360, 1679, 1644, 1584, 1439, 1208, 1171, 1043, 742, 691, 668; LC/MS $[M + H]^+$ 567.9, $[M + Na]^+$ 590.1.

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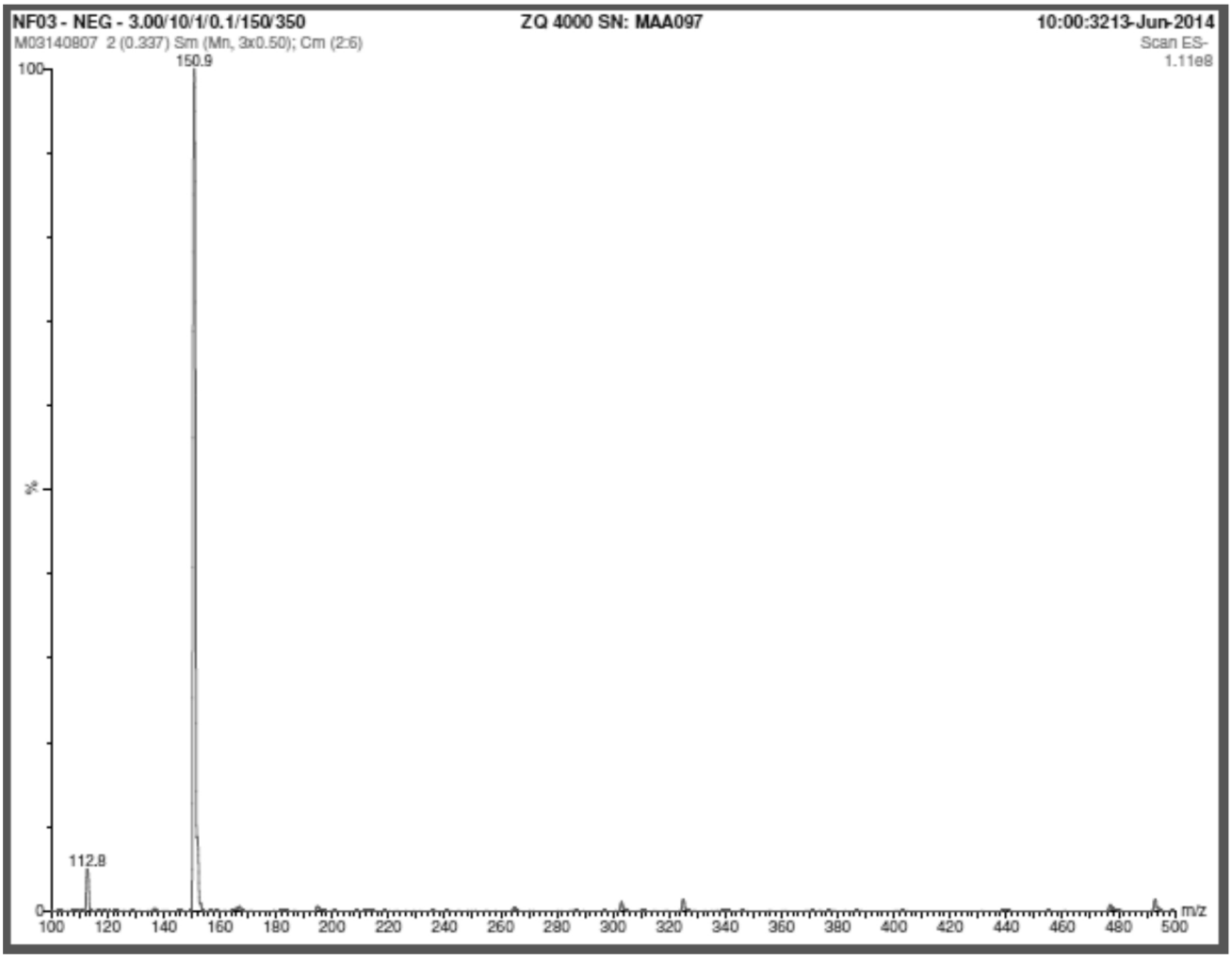

Figure S1. Mass spectrum of impurity A.

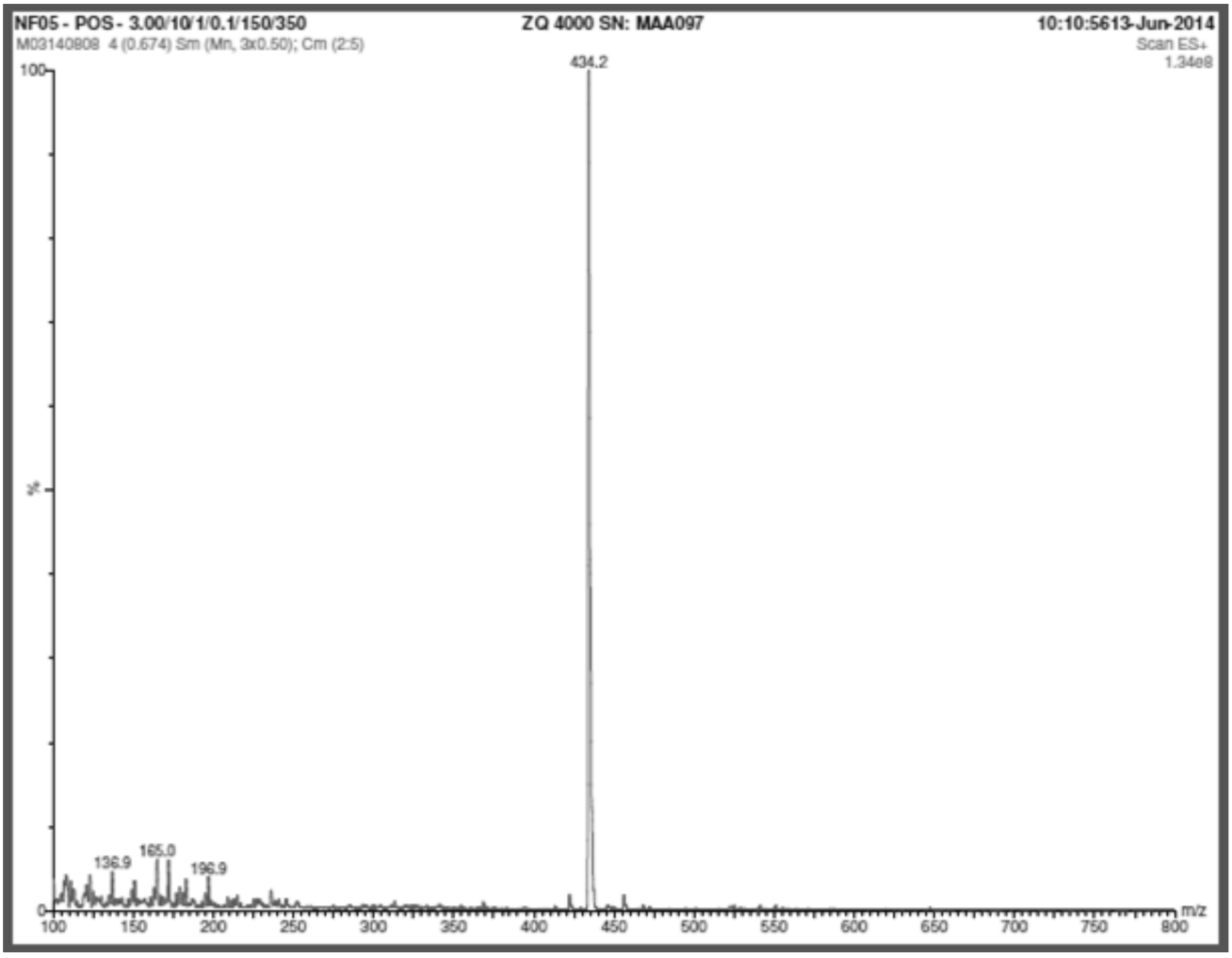

Figure S2. Mass spectrum of impurity B.

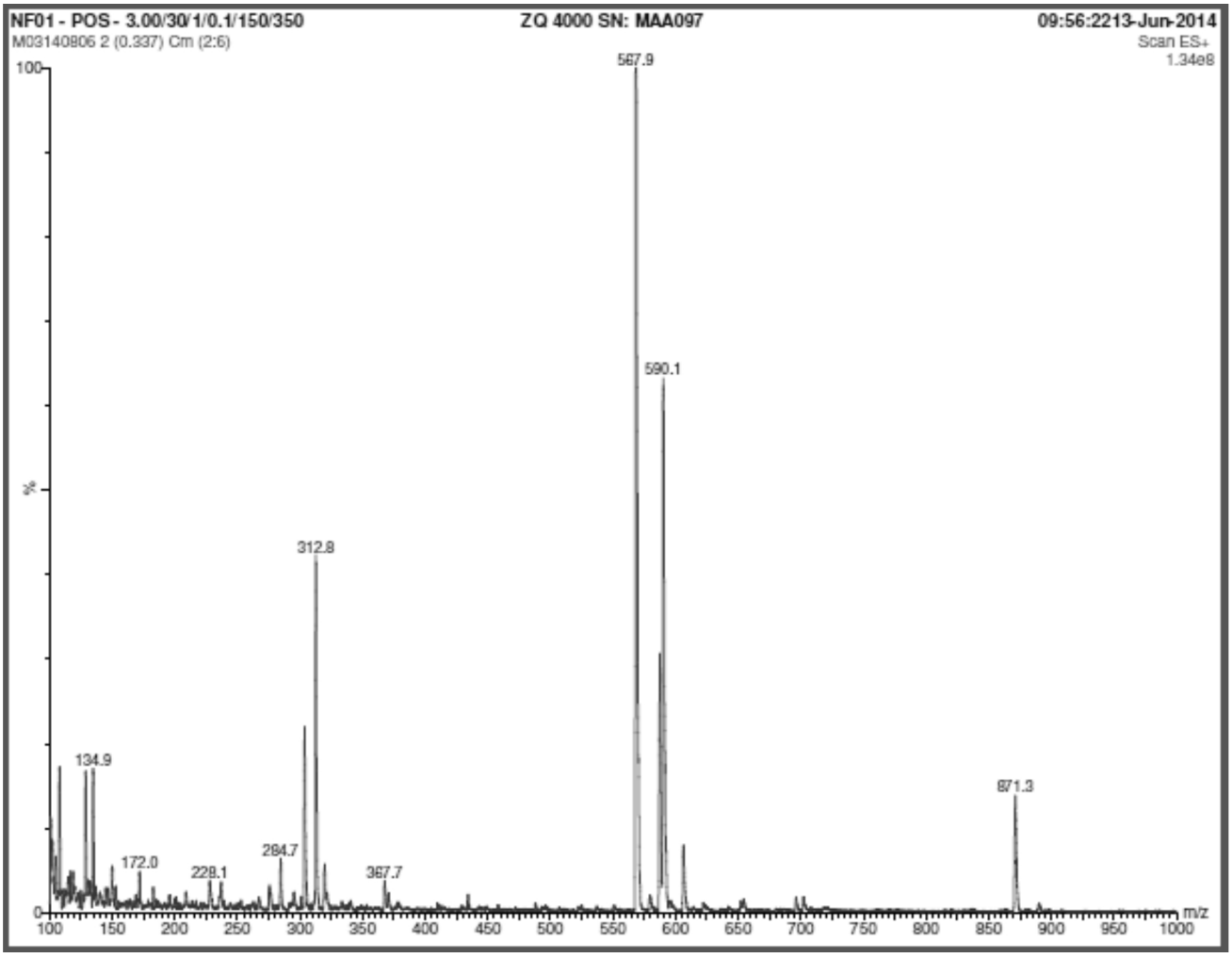

Figure S3. Mass spectrum of nelfinavir mesylate.