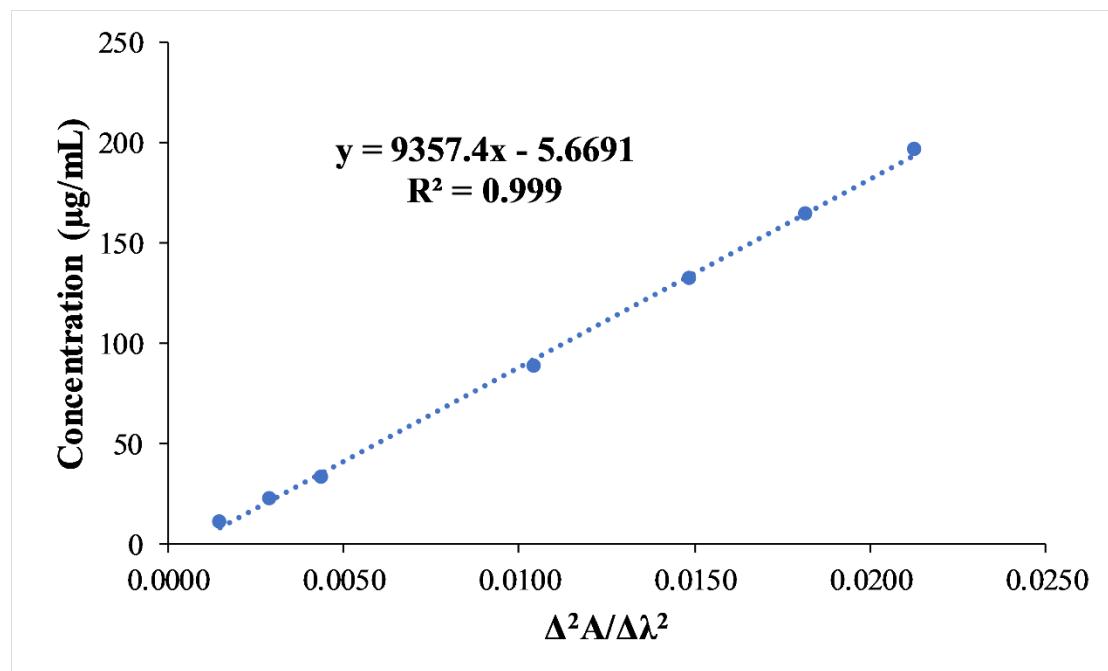


Towards more accurate solubility measurements with real time monitoring: a carvedilol case study

Dóra Csicsák,^a Enikő Borbás,^{*b} Szabina Kádár,^b Petra Tőzsér,^b Péter Bagi,^b Hajnalka Pataki,^b Bálint Sinkó,^c Krisztina Takács-Novák^a and Gergely Völgyi^a

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Supplementary Figure 1. Calibration curve of carvedilol at pH=6.5

Stability measurements

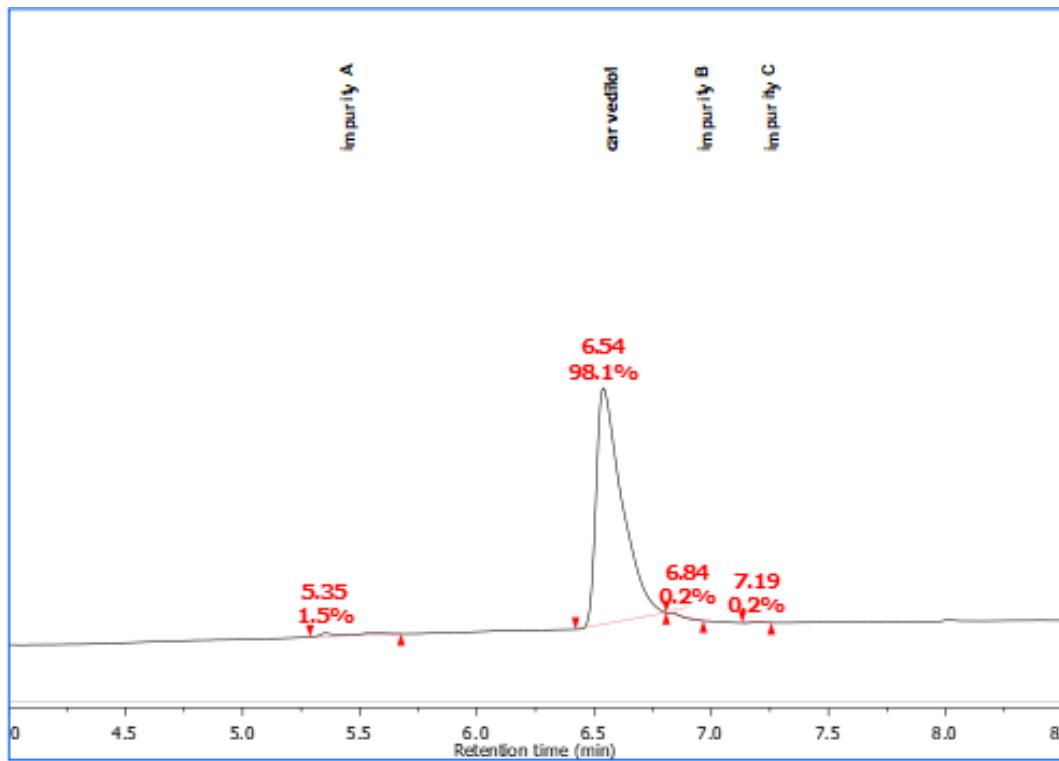
HPLC-MS was performed on an Agilent Technologies 1200 Series HPLC - Agilent Technologies 6130 Quadrupole MS in positive and negative electrospray mode; column: Phenomenex Kinetex C18 2.6 µm 100A 50 × 3.00 mm; column temperature: 40°C; flow rate: 0.5 mL/min; A eluent: water (0.1% HCOONH₄); B eluent: MeCN (8% water, 0.1% HCOONH₄); gradient: 10% eluent B from 0 to 1.0 min, linear gradient to 90% eluent B from 1.0 min to 6.0 min, 90% eluent B from 6.0 min to 10.0 min, followed by a linear gradient back to 10% eluent B from 10.0 to 15.0 min; UV detector: α 280 nm.

Supplementary Table 1: HPLC data for the stability tests of carvedilol Form I and II.

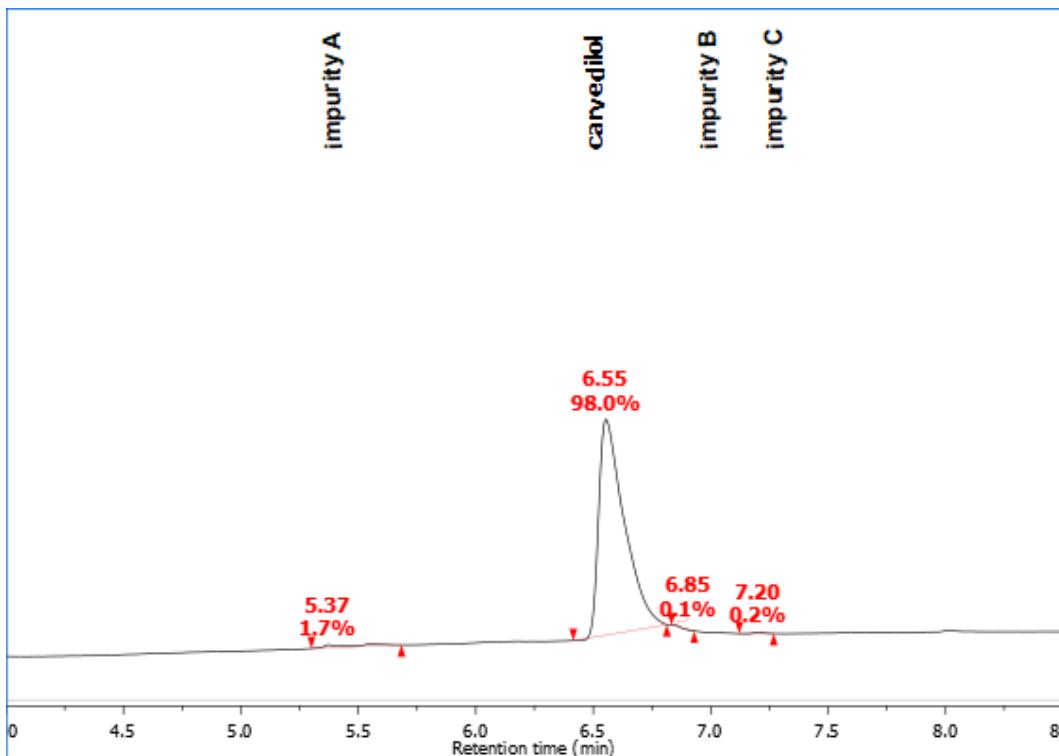
Entry	Sample	Carvedilol (%)	Impurity A (%)	Impurity B (%)	Impurity C (%)
1	Form I. pH=4 BR	97.5	1.8	0.4	0.3
2	Form I. pH=4 BR+KCl	98.1	1.5	0.2	0.2
3	Form I. pH=6 BR	99.4	n.d.	n.d.	0.6
4	Form I. pH=6 BR+KCl	98.5	1.1	0.2	0.2
5	Form II. pH=4 BR	98.5	0.8	0.4	0.3
6	Form II. pH=4 BR+KCl	98.0	1.7	0.1	0.2
7	Form II. pH=6 BR	98.8	1.0	0.1	0.1
8	Form II. pH=6 BR+KCl	99.4	0.6	n.d.	n.d.

Representative HPLC chromatograms

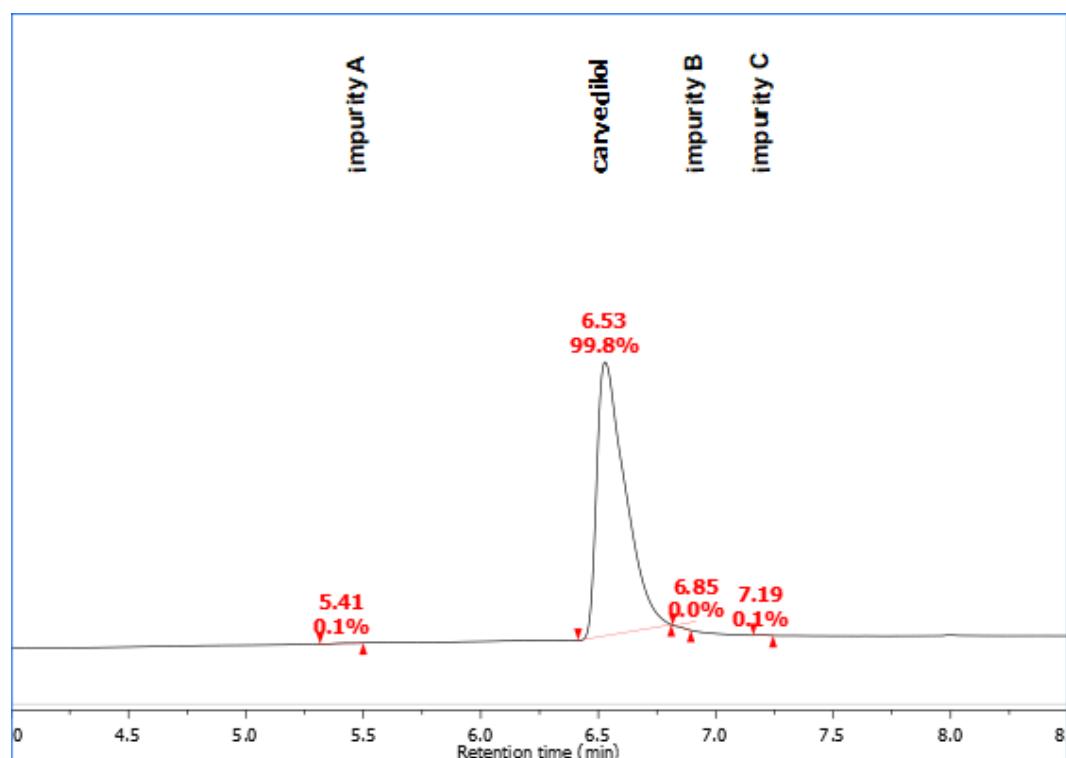
Form I. pH=4 BR+KCl (Supplementary Table 1, Entry 2)



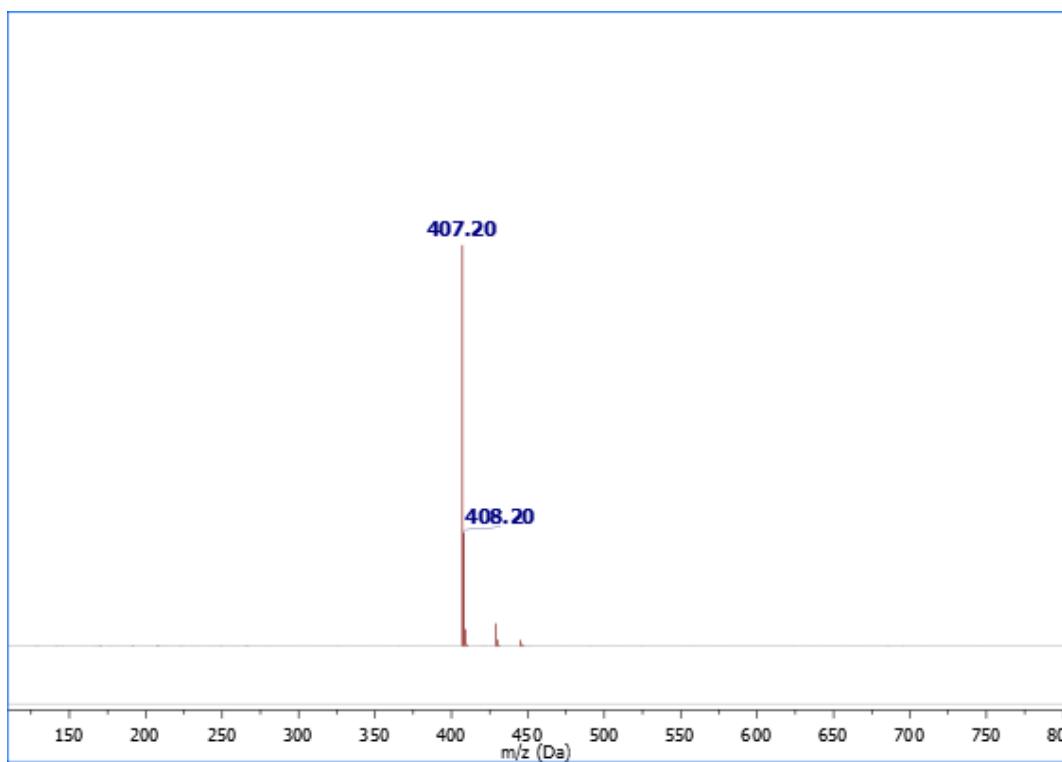
Form II. pH=4 BR+KCl (Supplementary Table 1, Entry 6)



carvedilol standard



Representative mass spectra of carvedilol.



Based on the HPLC-UV and HPLC-MS measurements no significant detectable degradation of carvedilol (<2.5%) was observed.