Supporting information

Developmental considerations for ethanolates with regard to stability and physicochemical characterization of efonidipine hydrochloride ethanolate

Masafumi Otsuka[1], Yusuke Maeno[1], Toshiro Fukami[2], Tatsuaki Tagami[3], Tetsuya Ozeki[3]

[1]Analysis Research Department, Nissan Chemical Industries, Ltd.
[2]Department of Molecular Pharmaceutics, Meiji Pharmaceutical University
[3]Graduate School of Pharmaceutical Sciences, Nagoya City University

Supporting information

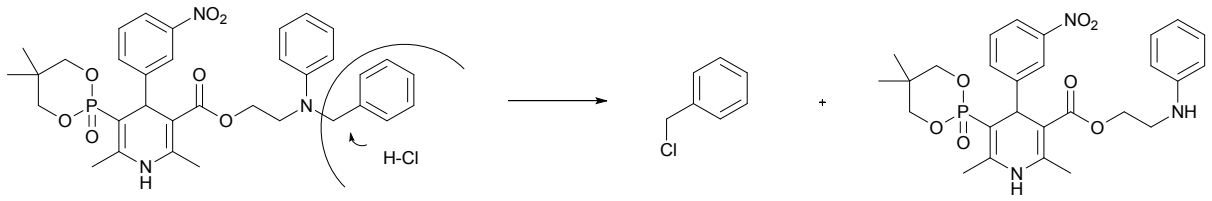

Figure S1. Degradation pathway for efonidipine hydrochloride ethanolate

Table S1. Particle size data for efonidipine hydrochloride ethanolate

Lot No.	10%volume cumulative diameter (μm)	50%volume cumulative diameter (μm)	90%volume cumulative diameter (μm)	Average particle diameter (μm)	Most frequent diameter (μm)
H02N01	10.049	23.614	53.359	22.538	26.230
H04N01	9.411	25.498	62.775	23.943	26.231
H08K12	10.284	28.589	70.878	24.985	32.381
H09K12	8.054	26.520	80.746	24.412	26.231
H10H09	8.145	27.418	66.339	23.865	32.381
H28C11	14.516	33.603	61.908	30.002	39.973

3. Experimental condition for stability test

Related substance: HPLC

Instrument: LC-20 series (Shimadzu, Kyoto, Japan)
Detector: Ultraviolet absorption photometer (wave length 254 nm)
Column: Spherisorb ODS-2 (I.D.5 mm × Length 25cm, P.D.5 μm: Waters, Tokyo, Japan)
Column temperature: A constant temperature about 40°C
Mobile phase: MeOH 400 mL/Acetonitrile 300 mL/0.1 mol/L aqueous ammonium acetate solution 300 mL with Tetra-n-butylammonium bromide 1.6 g.

HCl content: Titration (0.05 moL/L aqueous silver nitrate solution)

Instrument: AT400-win (Kyoto electronics manufacturing, Kyoto, Japan)

EtOH content: GC and Head space

GC condition
Instrument: Agilent 6890N (Agilent technologies, Tokyo, Japan)
Detector: Hydrogen flame ionization detector
Column: DB-624 (30 m × 0.32 mm, I.D. 1.8 μm: Agilent technologies, Tokyo, Japan)
Column temperature: Injection at a constant temperature about 40°C, maintain at 40°C for 10 min, raise the temperature to 130°C at a rate 10 °C/min, raise to 250°C at a rate 60°C/min, and maintain at 250°C for 9 min.
Inlet temperature: A constant temperature about 250°C
Detector temperature: A constant temperature about 250°C
Career gas: Helium
Flow late: 1.4 mL/min

Head space condition
Instrument: Turbo Matrix HS-40 (PerkinElmer, Kanagawa, Japan)
Vial equilibrium temperature: A constant temperature about 80°C
Vial equilibrium time: 60 min
Inlet line temperature: A constant temperature about 150°C
Pressure time: 3.0 min
Inlet time: 0.15 min

Assay: Titration (0.1 moL/L perchloric acid)

Instrument: AT400-win (Kyoto electronics manufacturing, Kyoto, Japan)