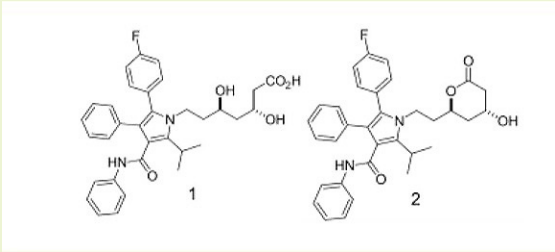
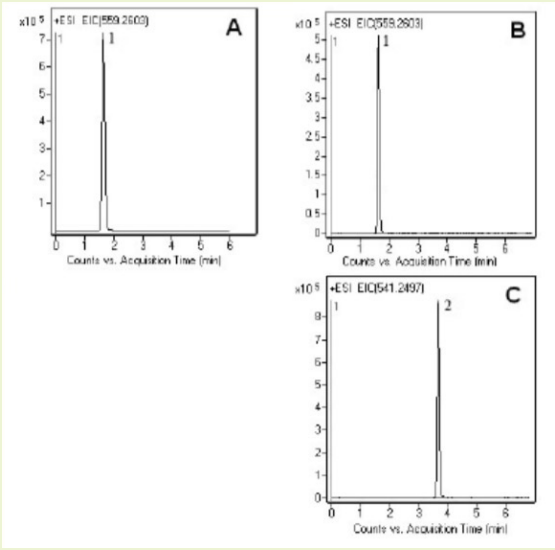
Forced Degradation of Atorvastatin (LC-MS)

Separation of API from its lactone degradation product





Note: Atorvastatin is a competitive inhibitor of 3-hydroxy-3-methlyglutaryl coenzyme A (HMG-CoA) reductase, which catalyzes the rate-limiting step in cholesterol biosynthesis. As such, atorvastatin is used to reduce plasma levels of low-density lipoprotein (LDL) cholesterol, which are known to contribute to the development of atherosclerosis. Atorvastatin is currently marketed by Pfizer under the trade name Lipitor, with the U.S. patent set to expire in November 2011.

Method Conditions

Column: **Cogent Bidentate C18™**, 4µm, 100Å

Catalog No.: 40018-05P-2

Dimensions: 2.1 x 50 mm

Solvents: A: 50% DI H_2O/ 50% methanol/ 10 mM ammonium acetate
B: 90% Acetonitrile/ 10% DI H_2O/ 10 mM ammonium acetate
Both Solutions were vacuum filtered through a 0.45µm nylon filter (MicroSolv Technology Corp.)

Gradient:

time (min.)	%B
0	30
10	100
12	30

Flow rate: 0.4 mL/min

Detection: ESI — POS - Agilent 6210 MSD TOF mass spectrometer

Sample: **Tablet Stock Solution:** A 40 mg strength tablet was ground and added to a 100 mL volumetric flask. A 50 mL portion of solvent B was added to the flask. The solution was vortexed 5 min, sonicated 5 min, and diluted to mark with solvent A. It was then filtered through a 0.45µm nylon membrane (MicroSolv Technology Corp.).

Degraded Tablet Stock Solution: A 40 mg strength tablet was ground and added to a 100 mL volumetric flask. A 50 mL portion of solvent B was added to the flask. It was then vortexed 5 min, sonicated 5 min, and diluted to mark with 3 M HCl. It was then filtered as above

Fig. A: 10µL tablet stock diluted with 990µL 50:50 A:B
Fig. B and C: 10µL degraded tablet stock diluted with 990µL 50:50 A:B

Peaks: 1. Atorvastatin
2. Atorvastatin lactone

Discussion

Atorvastatin is separated from its main degradation product using a Bidentate C18 column and a simple linear reversed phase gradient. With the use of LC-MS, the identity of the degradant can be confirmed from its m/z value. The degradation is an intramolecular Fischer esterification, which is catalyzed under acidic conditions. Figure A shows the extracted ion chromatogram (EIC) corresponding to atorvastatin for the non-degraded extract. Figures B and C show the EICs of atorvastatin and the lactone degradant respectively for the acid-degraded extract.

MANUFACTURED BY:
MICROSOLV TECHNOLOGY CORPORATION
9158 Industrial Blvd NE
Leland, NC 28451
p: 1.732.380.8900
f: 1.910.769.9435
customers@mtc-usa.com
www.Cogent-HPLC.com