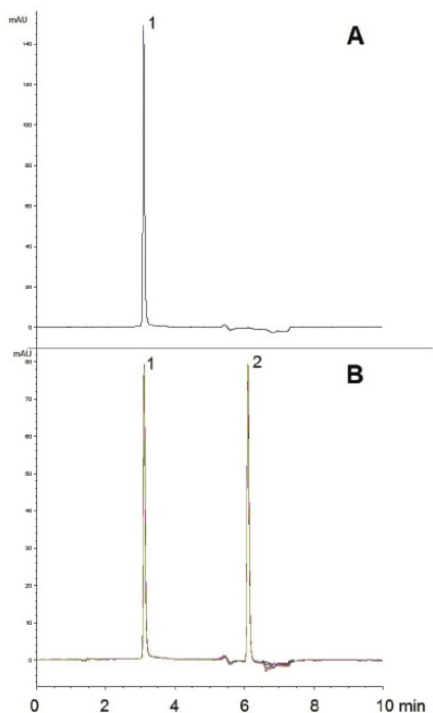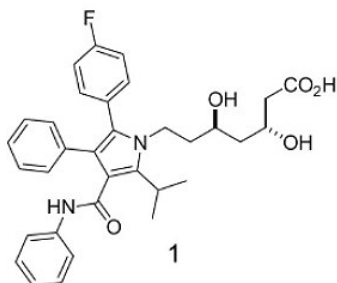**COGENT** Bidentate C18™

Forced Degradation of Atorvastatin
Separation of API from its main 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 toexpire in November 2011

Method Conditions

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

Catalog No.: 40018-15P

Dimensions: 4.6 x 150 mm

Solvents: A: DI H_2O/ 10 mM ammonium acetate
B: 90% Acetonitrile/ 10% DI H_2O/ 10 mM ammonium acetate

Gradient:

time (min.)	%B
0	40
5	100
6	40

Injection vol.: 2µL

Flow rate: 0.8 mL/min

Detection: UV 248 nm

Sample: A: Atorvastatin tablet extract
B: Degraded atorvastatin tablet extract
40 mg strength tablet ground, dispensed in 50 mL B in 100 mL volumetric flask. Vortexed 5 min, sonicated 5 min, then diluted to mark with A. Filtered through a 0.45µm nylon membrane (MicroSolv Technology Corp.). Diluted 4x with A) 50:50 A:B or B) 1.0 N HCl in 50:50 A:B.

Peaks: 1. Atorvastatin
2. Degradant

Discussion

Atorvastatin is separated from its main degradation product using a Bidentate C18 column and a simple linear reverse phase gradient. The degradant is formed under acidic conditions and therefore its separation is important for stability indicating methods for pharmaceutical formulations of atorvastatin. For methods requiring non-degrading conditions, it is important to choose diluent and mobile phase conditions with this pH sensitivity in mind. As such, ammonium acetate was chosen for the diluent and mobile phase additives in order to avoid any degradation from these sources. Data obtained under non-degrading conditions is shown in Figure A. Figure B shows an overlay of five consecutive runs of the degraded extract. The repeatability of the method is demonstrated by the low atorvastatin retention time %RSD of 0.10.