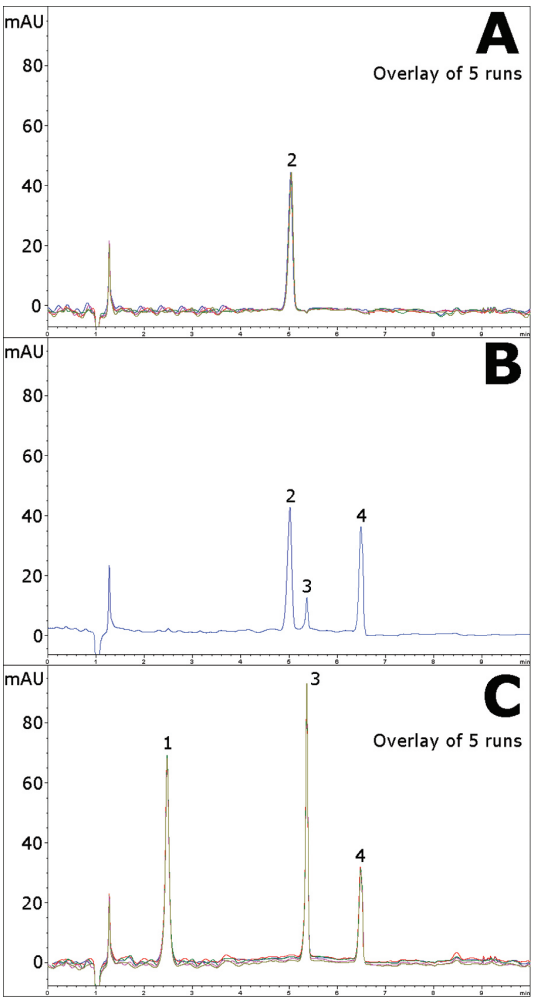
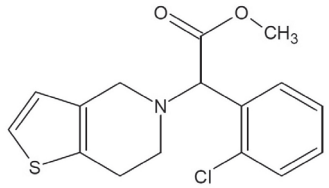
Forced Degradation of Clopidogrel

LC-MS compatible separation of API from degradants





Clopidogrel

Note: Clopidogrel is an antiplatelet agent used to inhibit blood clots, sold under the trade name Plavix.

Method Conditions

Column: **Cogent Diamond Hydride™**, 4µm, 100Å

Catalog No.: 70000-7.5P

Dimensions: 4.6 x 75 mm

Mobile Phase: A: DI H_2O / 0.1% formic acid (v/v)
B: Acetonitrile / 0.1% formic acid (v/v)

Gradient:

time (min.)	%B
0	95
2	95
7	60
8	95

Post Time: 2 min

Injection vol.: 1µL

Flow rate: 1.0 mL/min

Detection: UV 225 nm

Figures: **A:** Non-degraded extract: The stock solution was diluted 1:10 with 50/50 solvent A/solvent B mixture. Only the API peak is observed.
B: Base degradation: The stock solution was diluted 1:10 with 50/50 1N NaOH/Acetonitrile mixture. Two degradants are now present.
C: Base degradation with heating: The stock solution was diluted 1:10 with 50/50 1N NaOH/Acetonitrile mixture and then heated at 85°C for 30 min. The API peak is no longer observed but a third degradant (Peak 1) is now present.

Samples: Stock Solution: 50 mg strength Plavix® tablet was ground and diluted in 50/50 solvent A / solvent B mixture to 50 mL. The solution was sonicated and filtered through a 0.45µm nylon syringe filter (MicroSolv Tech Corp.).

Peaks: 1. Degradant
2. Clopidogrel (API)
3. Degradant
4. Degradant

t_0: 0.9 min

Discussion

Although clopidogrel, commonly known as Plavix, retains well in reverse phase, its degradants showed low retention even at high water content. Therefore a method using the Cogent Diamond Hydride column was used in which the compounds are retained on the basis of polarity. This method uses MS compatible solvents and provides excellent retention and separation between the API and three observed degradants.

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