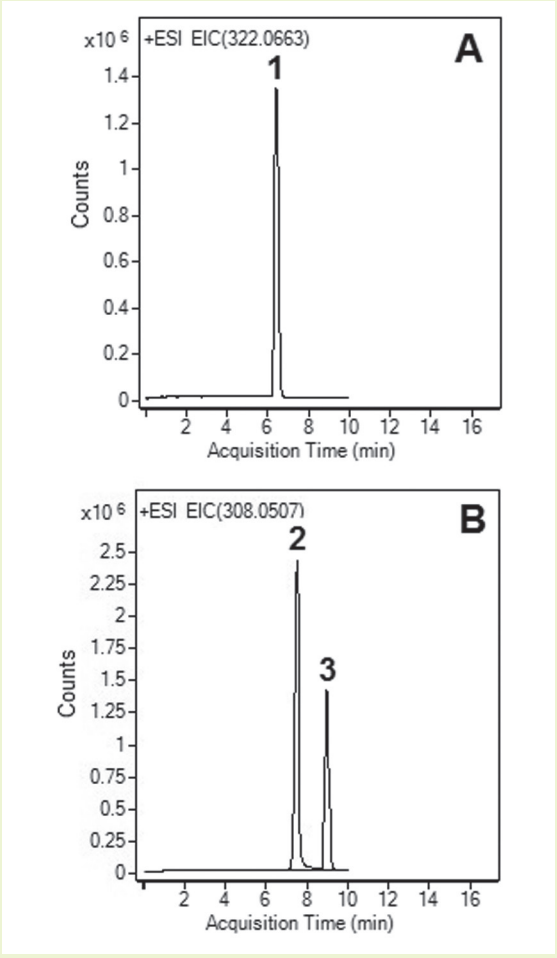
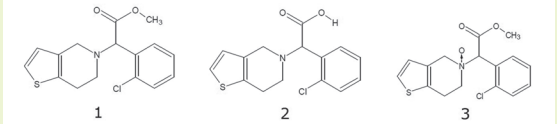
Forced Degradation of Clopidogrel with LC-MS

Separation of API and degradants





Figures: Fig. 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.
Fig. B: 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 degradants (Peak 2 and 3) are now present.

Method Conditions

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

Catalog No.: 70000-15P-2

Dimensions: 2.1 x 150 mm

Solvents: 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

Temperature: 25˚C

Post Time: 3 min

Injection vol.: 1µL

Flow rate: 0.4 mL/min

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

Sample: 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. API: Clopidogrel, m/z 322.0663 $[M+H]^+$
2. Degradant: Clopidogrel Acid, m/z 308.0507 $[M+H]^+$
3. Degradant: Clopidogrel N-oxide, m/z 338.02 $[M+H]^+$

t_0: 0.9 min

Discussion

A sensitive, selective, and rapid ANP HPLC–MS method was developed for the simultaneous quantification of clopidogrel (Plavix) and its degradants. Separation of the drug and the degradation products under stress conditions was successfully achieved on a Cogent Diamond Hydride column. The method was transferred from UV-HPLC method. The developed method can be used for the determination of clopidogrel in commercial tablets for quality control with an application to a content uniformity test. The method is also stability-indicating as it is suitable for the determination of clopidogrel in the presence of its degradation products under all stress conditions using HCl, NaOH, light and hydrogen peroxide.

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