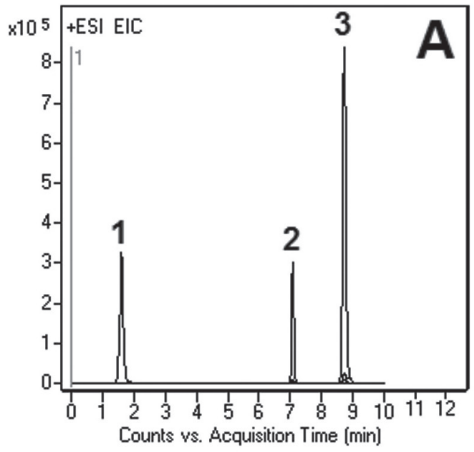
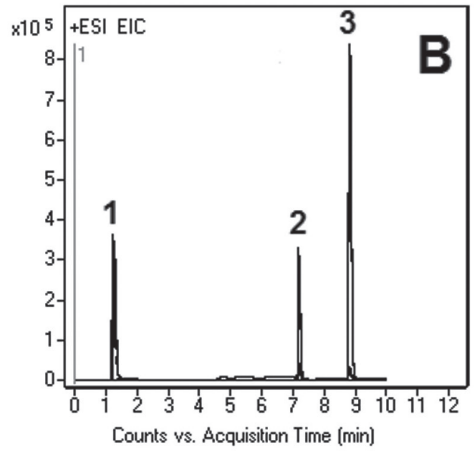
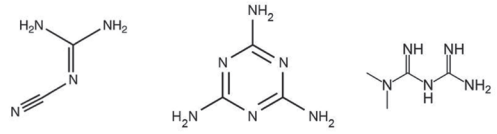
Impurities Method for Metformin HCL Formulation

Simple separation of API from melamine and cyanoguanidine







1. Cyanoguanidine 2. Melamine 3. Metformin

Note: k′ of cyanoguanidine for this method was found to be over twice that of strong reverse phase methods studied. The reverse phase methods used an ordinary cyano column with an isocratic mobile phase 95% DI H_2O / 5% acetonitrile. A variety of mobile phase additives were investigated, including 0.1% formic acid, 0.1% TFA, 0.1% TFA + 1 g/L Na octyl sulfate, and 10 mM ammonium acetate. None of the reverse phase methods produced k′ > 0.3.

Method Conditions

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

Catalog No.: 70000-15P-2

Dimensions: 2.1 x 150 mm

Solvents: A: 50% isopropanol / 50% DI H_2O / 0.1% acetic acid
B: Acetonitrile / 0.1% acetic acid

Gradient:

time (min.)	%B
0	100
2	100
5	20
9	20
10	100

Post Time: 5 min

Injection vol.: 1µL

Flow rate: 0.4 mL/min

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

Peaks: 1. Cyanoguanidine 85.0509 m/z $(M+H)^+$
2. Melamine 127.0727 m/z $(M+H)^+$
3. Metformin 130.1087 m/z $(M+H)^+$

Discussion

A simple method was developed for the analysis of the widely prescribed anti-diabetic drug metformin hydrochloride and for determination of two impurities (cyanoguanidine and melamine) in tablet formulations. This method has the ability to separate metformin from its impurities.

In addition to accurate mass for all three compounds, the peaks were confirmed by injections of standards. The USP-specified impurity limits are not more than 0.02% and 0.01% for cyanoguanidine and melamine respectively.

The precision of this method was evaluated by calculating %RSD of the peak areas of five replicate injections (see Figure B). The obtained value was 0.2%.

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