Waters Integrity System Applications

The Use of the Waters Integrity System for the Identification of Minor Impurities in Prochlorperazine

Highlights: Detection and identification of Prochlorperazine impurities using combined PDA/MS detection and automated library search capabilities.

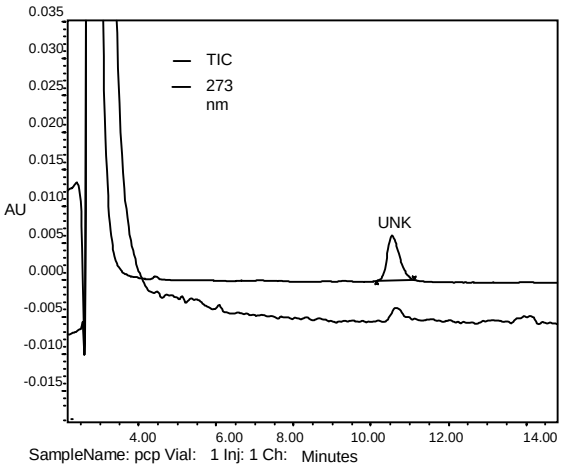
The identification of impurities in compounds is of paramount importance in many industries. What follows demonstrates the use of the Integrity system for the detection and identification of such impurities in Prochlorperazine, a tranquilizer. Prior to LC/MS analysis, no explanation could be found as to why the impurity was a much higher MW than the active compound. Information from the PDA detector showed that the spectra of the drug and the impurity were similar. The increase in MW could also not be explained by oxidation.

Prochlorperazine Experimental Conditions:

Waters Integrity System
- ThermaBeam mass detector
- 996 Photodiode Array detector
- 2690 Separations Module
- Millennium 2010 Chromatography Manager

LC Conditions
- Mobile Phase: 70% 20mM Ammonium: Acetate 30% Acetonitrile @ 0.25ml/min
- Column: Waters Symmetry C-8 150 X 2.1 mm ambient temp.
- PDA : 190-450nm @ 1.2 nm resolution
- TMD: 65-650 Da

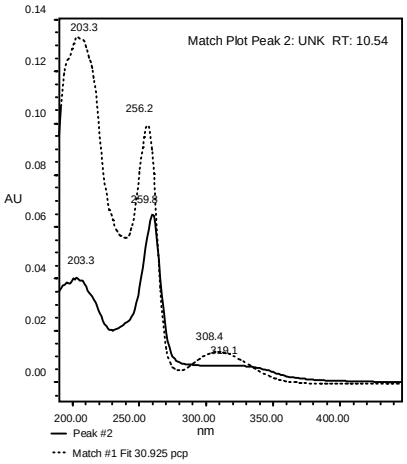
Prochlorperazine with Impurity



This diagram shows the overlay of the TIC with the UV chromatogram at 273 nm. Since these two traces overlay almost perfectly, there is very little loss of chromatographic resolution through the interface.

Positive compound identification is achieved through the ability of Integrity to generate Electron Ionization (EI) spectra on chromatographic peaks. The dual detector capability of Integrity also enhances compound ID. The system ensures low dispersion allowing a greater degree of well characterized peaks along with the ability to overlay the PDA and MS chromatograms for identification purposes. The PDA is very useful in this example since it was used to determine that the impurity is related to Prochlorperazine. There is also a need to confirm compound ID by more than one analytical technique, so LC/MS, in general, has been experiencing increasing interest.

UV Spectral Overlays



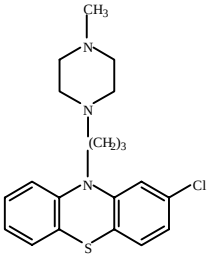
UV spectra of unknown and Prochlorperazine have similar spectral features

Here we see the overlay of the UV spectrum of the impurity and the library spectrum of Prochlorperazine. While the match is not a good match, it is clear that the spectra are related and, therefore, the impurity is probably a related compound. The three maxima for each compound are all very close in lambda max.

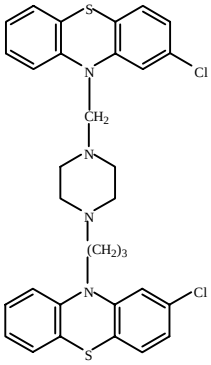
Prochlorperazine and its Impurity

This illustration shows the structure of Prochlorperazine along with a proposed structure of the unknown. The synthesis of the Prochlorperazine is made from methyl, propyl piperazine and chlorophenothiazine. It is not unreasonable to expect the addition of the chlorophenothiazine at the methyl group of the methyl propyl piperazine . This would yield the structure shown with a MW of 604.

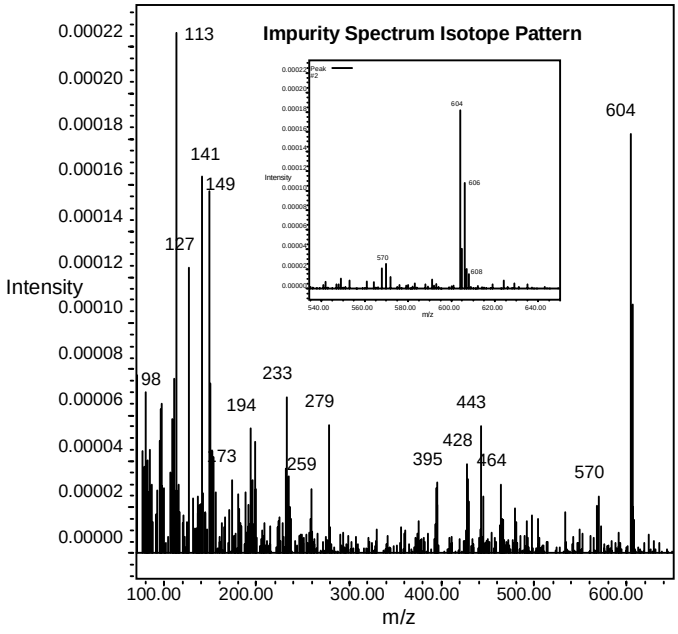
Prochlorperazine (PCP) mw 373



0.1% Impurity of Prochlorperazine



Mass Spectrum of Unknown



The mass spectrum of the unknown at 10.6 min. shows a molecular ion at m/z 604, 231 mass units higher than Prochlorperazine. This spectrum was searched against the Wiley library with no possible matches returned. The expanded region of the mass spectrum of the unknown has an isotope pattern for the molecular ion that is indicative of two chlorine atoms in the molecule. That is also consistent with the proposed structure.

By utilizing all of the chromatographic, mass spectral and PDA information available from the Integrity System, confidence in positive peak identification can easily be achieved.