Xevo TQ Absolute

[INDIA DEMO LAB]

A Robust and Sensitive Instrument for Quantification of Seven Nitrosamine Impurities in Quetiapine Drug Substance

INTRODUCTION:

Quetiapine is known as an anti-psychotic drug. It is primarily used to treat schizophrenia or bipolar disorder. In 2020, it was the 64th most prescribed medication in the United States. However, the discovery of nitrosamine impurities in some drug products led FDA to conduct a detailed root cause analysis of these impurities. These impurities might infiltrate in APIs and drug products due to use of vulnerable processes and materials that may produce nitrosamine impurities. Therefore, the recommendations made by FDA to monitor and control these impurities apply to all chemically synthesized APIs and to drug products at risk. Consequently, there is a need of highly sensitive LC/MS/MS method for the quantification of Nitrosamine Impurities in Quetiapine API.

SCOPE OF WORK:

The presented work demonstrates the analysis of seven Nitrosamine Impurities in Quetiapine drug substance using a single method. Waters Xevo TQ Absolute coupled with Acquity UPLC H-Class Plus along with HSS T3, 2.1 X 100 mm, 1.8 µm column provides a complete solution to overcome the challenges involved in such analysis. The developed method produces reproducible results at concentration as low as 0.003 ppm concentration (LOQ) with respect to the API. The observed recovery in spiked API was within 70 to 120% for all the seven nitrosamine impurities adapting extraction approach.

RADAR scan: Understanding sample complexity and matrix effect

RADAR is a unique tool on Waters Mass Detector that can acquire both MRM and full scan MS simultaneously without compromising sensitivity. This capability helps to understand matrix effect and offers the development of robust methods. It plays a key role in chromatographic separation of impurities from API, thereby enabling the diversion of API eluting at particular retention time to waste, avoiding mass detector contamination .

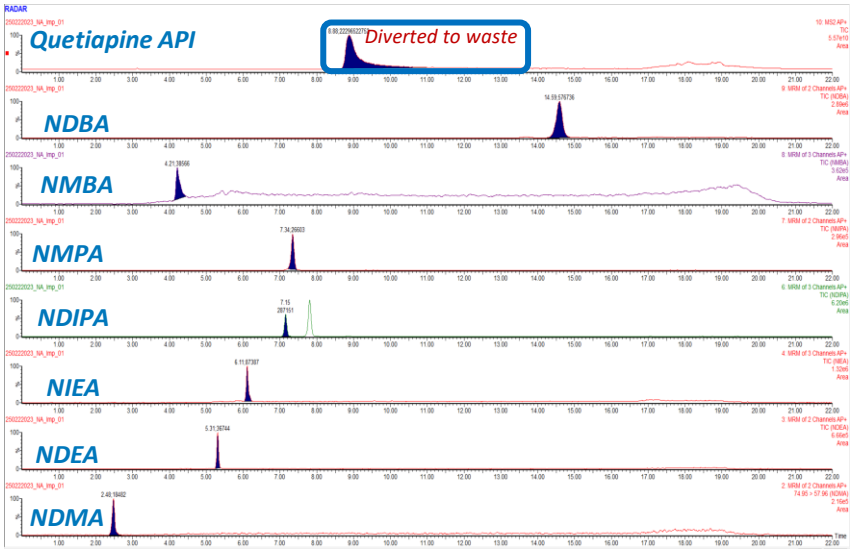

Figure 1. Chromatographic Separation of Nitrosamine Impurities from API

Figure 2: Xevo TQ Absolute with Acquity UPLC H-Class Plus

Method Performance Characteristics	
Linearity	0.0006 to 0.3 ppm
Method LOQ	0.003 ppm
Instrument LOQ	0.0006 ppm
Spiked Recovery	70 to 120 %

Table 1. Summary of method performance

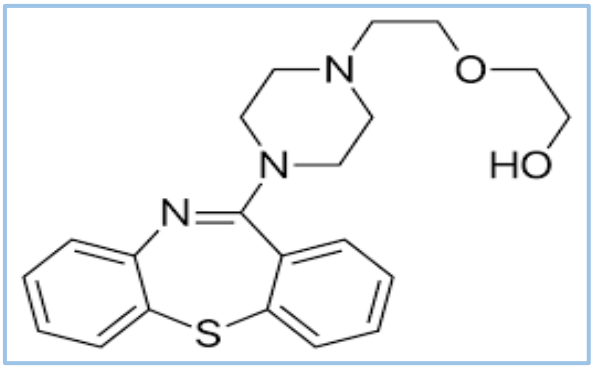

Figure 3: Quetiapine Chemical Structure

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