Xevo TQ-S Micro

[INDIA DEMO LAB]

A Robust and Sensitive Instrument for Quantification of N-Nitroso-N-Des Methyl Diltiazem Impurity in Diltiazem Drug Product

INTRODUCTION:

Diltiazem is a benzothiazepine derivative with antihypertensive and vasodilating properties. It is widely used for human consumption as a non-dihydropyridine calcium channel blocker. However, as per regulatory requirement, medicines which have possibility of forming Nitrosamine Drug Substance Related Impurities (NDSRIs) during manufacturing and/or storage, needs to be controlled. Due to the risk associated with such impurities, regulatory requirements are stringent which requires not only a highly specific analytical method but also a reproducible and sensitive detection technique.

SCOPEOFWORK:

In the present study, the performance of method based upon LC-MS/MS, using an ACQUITY H-Class Plus UPLC system coupled with Xevo TQ-S Cronos tandem quadrupole mass spectrometer, is demonstrated for the determination of N-Nitroso-N-Des methyl Diltiazem impurity in Diltiazem drug product. The separation of impurity was achieved using Atlantis™ Premier BEH C18 AX column. The developed method produced excellent sensitivity with S/N ratio >80 at 0.006 ppm level with respect to API and LOQ of 0.03 ppm. The observed spiked recovery was within 70 to 120 % by adapting extraction approach.

RADAR scan:

Understanding sample complexity, Intelligent method development & Understanding matrix effects

RADAR mode rapidly switches between MRM (MS/MS) mode and MS full scan acquisition which enables the analyst to monitor for matrix interferences, placebo, impurities and degradants in a sample while accurately quantifying target compounds without losing sensitivity or performance. *Figure 1* shows a RADAR scan investigation results where API is clearly separated from the NDSRI and eluting later. Diverting the API peak to waste, avoided the contamination of the mass spectrometer increasing the method robustness.

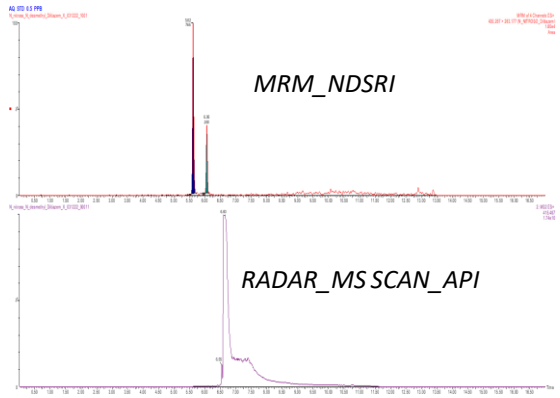

Figure 1. Chromatographic separation of N-Nitroso-N-Des methyl Diltiazem impurity and API by using RADAR scan

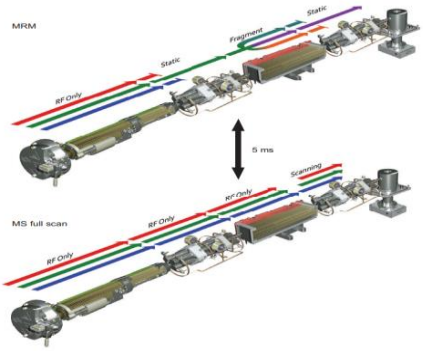

Figure 3: RADAR Functionality

Figure 2: Xevo TQ S Micro with Acquity UPLC H-Class Plus , Atlantis™ Premier BEH C18 AX 100 mm X 2.1 mm, 2.5 µm column

Test	Limit/Range
Linearity	0.006 to 5.0 ppm
Method LOQ	0.03 ppm
Instrument LOQ	0.006 ppm
Spiked recovery	82 %

Table 1. Summary of N-Nitroso-N-Des methyl Diltiazem impurity method performance

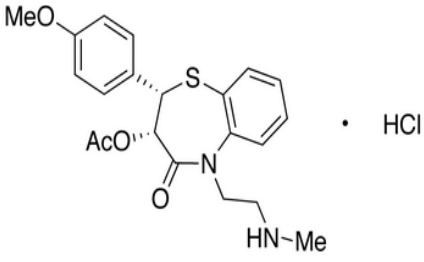

Figure 4: N-Nitroso-N-Des methyl Diltiazem

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