Xevo TQ-S Cronos

[INDIA DEMO LAB]

A Robust and Sensitive Instrument for Quantification of N-Nitroso Propranolol Impurity in Propranolol Hydrochloride Drug Product

INTRODUCTION:

Propranolol Hydrochloride is a synthetic beta-adrenergic receptor blocker with antianginal, antiarrhythmic, and antihypertensive properties. It is widely used as non-cardio selective beta-adrenergic antagonist. As per recent regulatory guidelines the selected drug products should be screened for Nitrosamine Drug Substance Related Impurities (NDSRI). These impurities are structurally similar to APIs and can be generated during the manufacturing or storage period of the drug product. Consequently, there is a need of highly sensitive LC/MS/MS method for the quantification of N-Nitroso Propranolol in Propranolol drug product.

SCOPE OF WORK:

The presented work overcomes the complications involved in NDSRI analysis and provides a complete analytical solution using Waters Xevo TQ-S Cronos coupled with Acquity UPLC H-Class Plus along with Symmetry C8 Column. The developed method for quantification of N-Nitroso propranolol impurity produced reproducible results with LOQ of 0.01 ppm with respect to API. The instrument shows excellent sensitivity with S/N ratio >70 at 0.002 ppm level. 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 is an acquisition mode that acquires both MRM and full scan MS simultaneously, a unique capability that can both simplify and accelerate development of robust methods. During method development, RADAR offers the ability to understand unexpected results due to matrix effects The *Figure 1* shows a Radar scan investigation results where API is clearly separated from the NDSRI and eluting later. Diverting the API peak avoided the contamination of the mass spectrometer increasing the method robustness.

Figure 2: Xevo TQ S Cronos with Acquity UPLC H-Class Plus , and Symmetry C8 Column

Test	Limit/Range
Linearity	0.002 to 2.0 ppm
Method LOQ	0.01 ppm
Instrument LOQ	0.002 ppm
Spiked recovery	84 %

Table 1. Summary for N-Nitroso propranolol impurity method performance

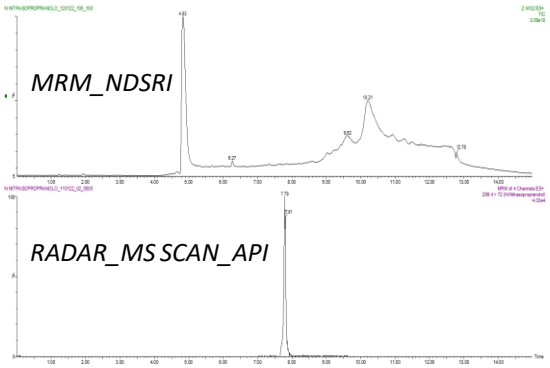

Figure 1. Chromatographic Separation of N-Nitroso propranolol impurity and formulation by using RADAR scan

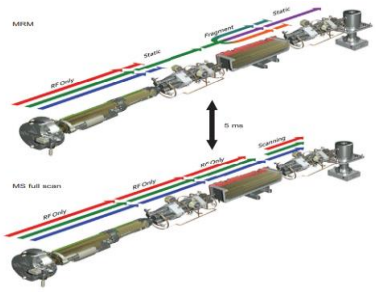

Figure 3: RADAR Functionality

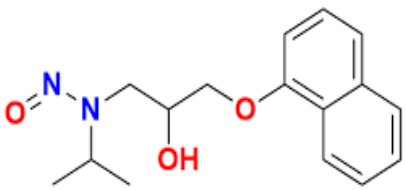

Figure 4: N-Nitroso propranolol

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