Xevo TQ-S Cronos

[INDIA DEMO LAB]

A Robust and Sensitive Instrument for Quantification of N-Nitroso labetalol impurity in Labetalol Drug Product.

INTRODUCTION:

A recently published general chapter in USP-NF, General Chapter <1469> Nitrosamine Impurities, identifies possible sources in drug products, their components and their manufacturing process, along with the risks associated with each source. These nitrosamine drug substance-related impurities (NDSRIs) are a class of nitrosamines sharing structural similarity to the API. In some cases, the root cause of NDSRI formation has been attributed to nitrite residues present in excipients at parts-per-million amounts. With many potential sources, it is critical that manufacturers evaluate their products for risks. Ensuring the control of a product's impurities levels cannot simply be a last step in the manufacturing process; manufacturers must pursue quality in the lifecycle of a drug from beginning to end.

SCOPE OF WORK:

To overcome the analytical challenges of matrix effect and to improve the spiked recovery for N-Nitroso labetalol impurity quantification in drug product needs a suitable sample preparation technique and chromatographic conditions. Waters Xevo TQ-S Cronos coupled with Acquity UPLC H-Class plus and Acquity UPLC BEH C18 Column combination produced robust method for quantification of N-Nitroso labetalol impurity at method LOQ 0.03 ppm and the instrument shows excellent sensitivity with S/N ratio (>300) at 0.003 ppm level with respect to API. The observed spiked recovery was between 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 without loss of sensitivity, 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 before NDSRI. Diverting the API peak avoided the contamination of the mass spectrometer increasing the method robustness.

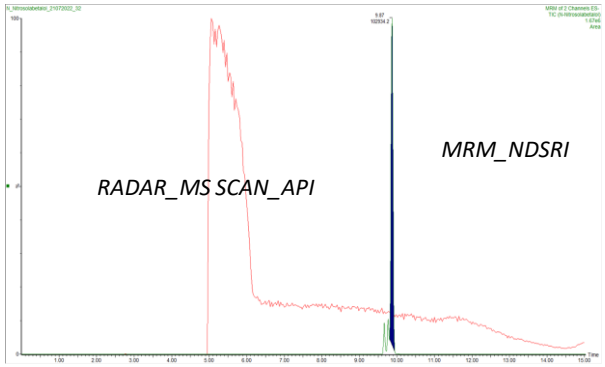

Figure 1. Chromatographic Separation of N-Nitroso labetalol *Impurity and formulation by using radar scan*

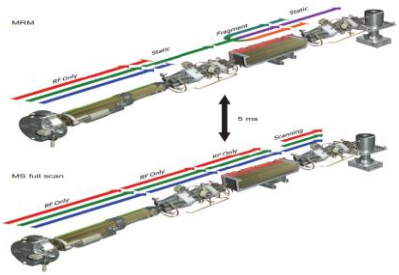

Figure 3: RADAR Functionality

Figure 3: Xevo TQ S Cronos with Acquity UPLC H-Class Plus , and Acquity UPLC BEH C18 Column

Test	Limit/Range
Linearity	0.003 to 1.5 ppm
Method LOQ	0.03ppm
Instrument LOQ	0.003 ppm
Spiked recovery	93.5 %

Table 1. Summary for N-Nitroso labetalol impurity

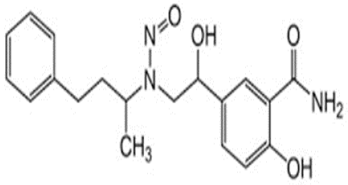

Figure 4: N-nitroso labetalol impurity

Waters ™