Xevo TQ-S Cronos

[INDIA DEMO LAB]

A Robust and Sensitive Instrument for Quantification of N-Nitroso Argatroban impurity at 0.3 ppm in Argatroban Drug Product.

INTRODUCTION:

Recently, FDA has received additional reports of certain types of nitrosamine impurities that formed in several drug products. These nitrosamine drug substance-related impurities (NDSRIs) are a class of nitrosamines sharing structural similarity to the API. NDSRIs can be generated during manufacturing or the shelf-life storage period of the drug product. In many cases, the root cause of NDSRI formation has been attributed to nitrite impurities present in excipients at trace amounts. Nitrite impurities have been observed in a range of commonly used excipients which may lead to the formation of NDSRIs in certain drug products.

Xevo TQ-S Cronos with Acquity UPLC H-Class Plus , and Acquity UPLC HSS T3 Column

SCOPE OF WORK:

To overcome the analytical challenges of matrix effect and to improve the spiked recovery for N-Nitroso argatroban impurity 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 HSS T3 Column combination produced robust method for quantification

N-Nitroso argatroban impurity method performance at LOQ of 0.3 ppm, the instrument showed excellent sensitivity with S/N ratio (>1000) at 0.05 PPM level with respect to API. The observed spiked recovery was between 70 to 120% by adapting extraction approach with minimal sample concentration.

Test	Limit/Range
Linearity	0.05 to 50 ppm
Method LOQ	0.3ppm
Instrument LOD	< 0.005 ppm
Spiked recovery	94 %

Table 1. Summary for N-Nitroso Argatroban Impurity

Radar scan:

Understanding sample complexity, Intelligent method development and minimizing the matrix effects.

RADAR is an acquisition mode that acquires both MRM and full scan MS simultaneously without compromising 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 later. Diverting the API peak avoided the contamination of the mass spectrometer increasing the method robustness.

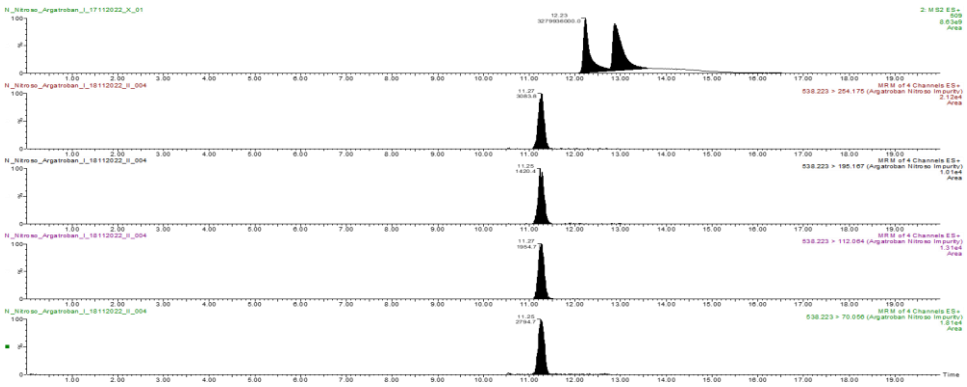

Figure 1. Chromatographic Separation of N-Nitroso Argatroban Impurity and formulation by using radar scan

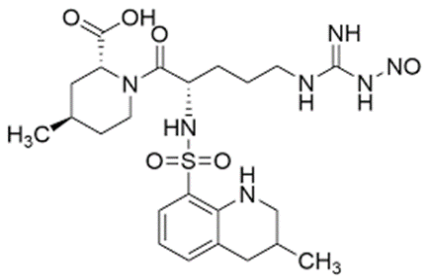

Figure 2. N-Nitroso Argatroban

Waters ™