Xevo TQ-S Cronos

[INDIA DEMO LAB]

A Robust and Sensitive Instrument for Quantification of N-nitroso Morpholine impurity in Mycophenolate Mofetil HCl Drug Product.

INTRODUCTION:

Mycophenolate is in a class of medications called immunosuppressive agents. It works by weakening the body's immune system so it will not attack and reject the transplanted organ. Mycophenolate is used with other medications to help prevent transplant organ rejection who have received kidney, heart, or liver transplants. Due to the risk of carcinogenic property N-Nitrosamine impurities are considered as concern for human consumption above acceptable limit. N-nitroso morpholine impurity is a related impurity of Mycophenolate Mofetil HCl. N-nitroso morpholine can be formed during manufacturing process and shelf-life storage period .

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

SCOPE OF WORK:

Due to the similar properties of N-nitroso morpholine impurity and Mycophenolate there is a challenge of loss of recovery due close elution of the impurity and the drug substance. The combination of optimized chromatographic conditions, Waters Xevo TQ-S Cronos coupled with Acquity UPLC H-Class plus and Acquity UPLC BEH C18 Column produced robust method for quantification of N-nitroso morpholine impurity at method LOQ 0.03 ppm and the instrument shows excellent sensitivity with S/N ratio (>100) at 0.015 ppm level with respect to API. The observed spiked recovery was within 70 to 120 % by adapting sample extraction approach.

Test	Limit/Range
Linearity	0.015 to 0.75 ppm
Method LOQ	0.03 ppm
Instrument LOQ	0.003 ppm
Spiked recovery	85 %

Table 1. Summary for N-nitroso morpholine impurity

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 later. Diverting the API peak avoided the contamination of the mass spectrometer increasing the method robustness.

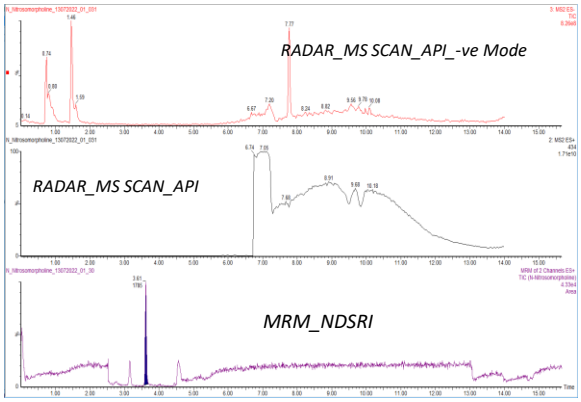

Figure 1. Chromatographic Separation of N-nitroso morpholine Impurity and formulation sample by RADAR scan

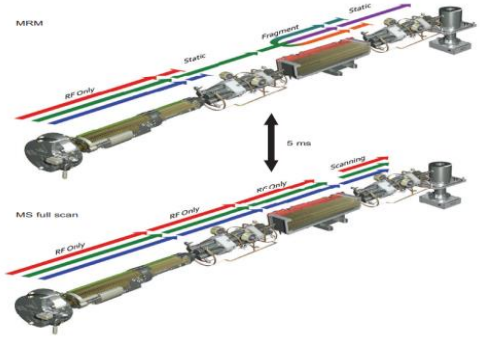

Figure 3: RADAR Functionality

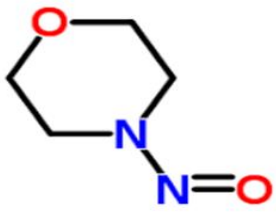

Figure 4: N-nitroso morpholine

Waters ™