Xevo TQ-Absolute

[INDIA DEMO LAB]

Waters Xevo TQ Absolute: An extremely sensitive LCMSMS for quantification of low concentration of seven Nitrosamine impurities

K Pavan Kumar , Taposh Kumar G, Dr. Padmakar Wagh

INTRODUCTION

Nitrosamine impurities are more concern in the drug products due to its carcinogenicity. The main source of these impurities is from but not limited to the reaction byproducts during the manufacturing process.

FDA had found nitrosamines first in Sartans followed by Ranitidine and lately Metformin a drug used to treat Type 2 Diabetes. Metformin is the main first-line medication for the treatment of type 2 diabetes, particularly in people who are overweight. It is also used in the treatment of polycystic ovary syndrome. It is not associated with weight gain and is taken by oral.

Regulators allow to eliminate the nitrosamines test from the product specification if the nitrosamine content found to be consistently less than 10-fold of specification limit, this provision raise the need for a method which can reach the sensitivity levels of typically 30-fold lower (0.001ppm) than the present regulatory limit (0.03ppm) considering the analytical uncertainty.

SCOPE OF WORK

Analytical challenge of chromatographic interference of metformin in the estimation of NDMA is critical as both are highly polar, eluting very close to each other, which results in low spiked recovery for the NDMA impurity.

Combination of extremely sensitive Xevo TQ Absolute with Acquity UPLC H Class plus and Acquity UPLC HSS T3 column produced excellent sensitivity. Metformin drug substance was spiked with seven nitrosamine impurities at 0.0005 ppm and the recovery found was between 88 to 111% by a simple sample extraction procedure.

The signal to noise ratio for seven nitrosamine impurities was found to >10 at the method LOQ of 0.0005ppm.

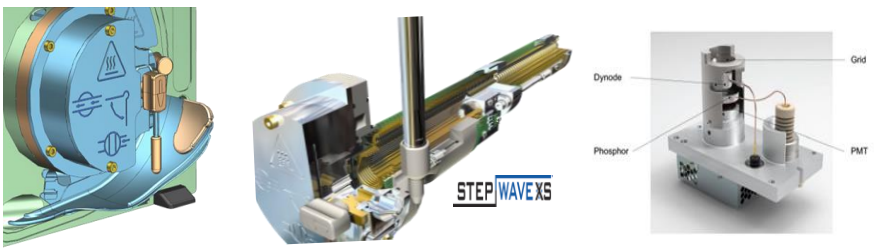

Figure 1: New removable source shield, Low noise Off axis robust StepWave Ion Guide and next gen photomultiplier XDR ™ Detector.

Xevo TQ Absolute with Acquity UPLC H-Class Plus

Limit Test	Limit/Range
Linearity	0.00025 to 0.25 ppm
Method LOQ	0.0005ppm
Spiked recovery	88 to 111%

Table 1.Results of seven Nitrosamine Impurities in Metformin drug substance

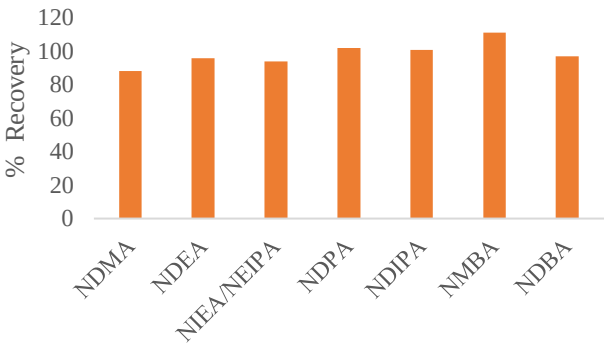

Figure 3. Recovery of Nitrosamine impurities spiked at 0.0005ppm

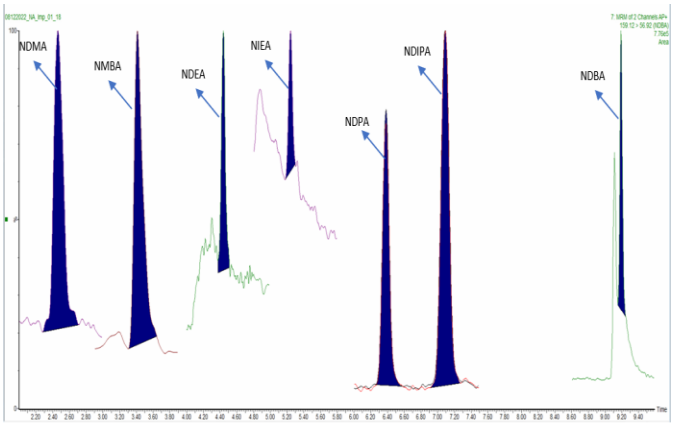

Figure 4. Chromatographic Separation of seven Nitrosamine Impurities.

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