



Analysis of Nitrosamines in Sartans by GC-TEA

Overview

This application note describes the analysis of nitrosamine contamination in Losartan tablets.

Background

Losartan is a commonly prescribed medication for managing high blood pressure and heart failure, with typical daily dosages ranging from 25 mg to 100 mg. In recent years, nitrosamine contamination in pharmaceuticals has raised significant concerns. Notably, N-Nitrosodimethylamine (NDMA), a probable human carcinogen. The acceptable daily intake limit for NDMA in pharmaceutical products is 96 nanograms. Monitoring NDMA levels in losartan is essential to maintain patient safety and comply with regulatory standards.

Analytical Method

Automated Total Nitrosamine Analysis (ATNA)

The ATNA system was employed to screen for nitrosamines in the metformin samples. ATNA uses a non-targeted approach to detect the NO functional group, which is common to all nitrosamines.

Calculations for Tablet Quantity

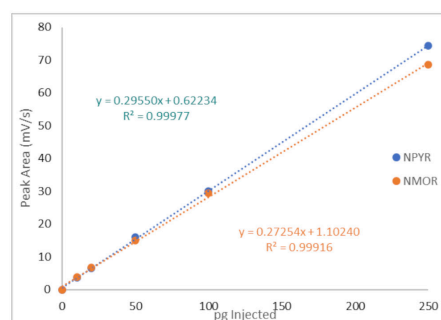
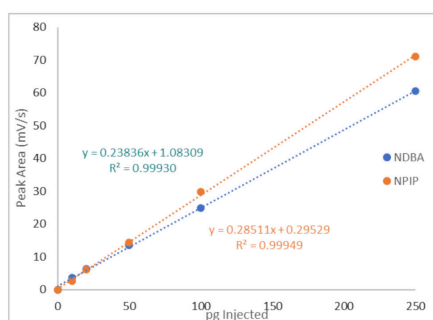
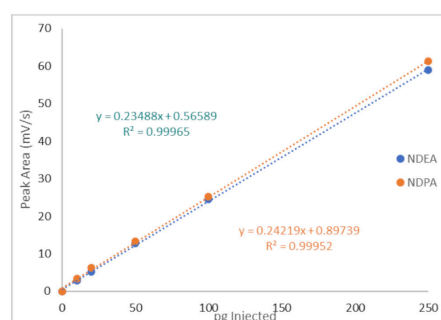
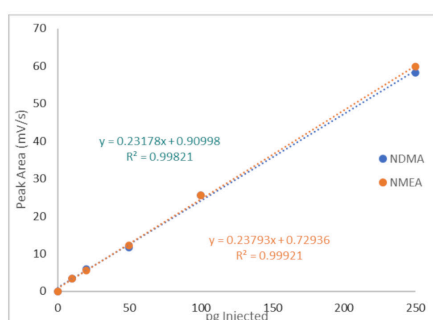
Determining the appropriate quantity of tablets to test depends on the sensitivity of the GC-TEA system for each nitrosamines. For instance, in Losartan, given a maximum daily dosage of 100mg, the FDA sets the NDMA daily limit at 96 ng. The GC-TEA can detect 40pg of NDMA on column. We inject 0.5µl of the methanol extracted sample.

With the standard extraction procedure (1 tablet with 1 ml of solvent), the threshold becomes 96ng in 1ml which equates to, 96pg per µl or 48 pg in 0.5 µl injection.

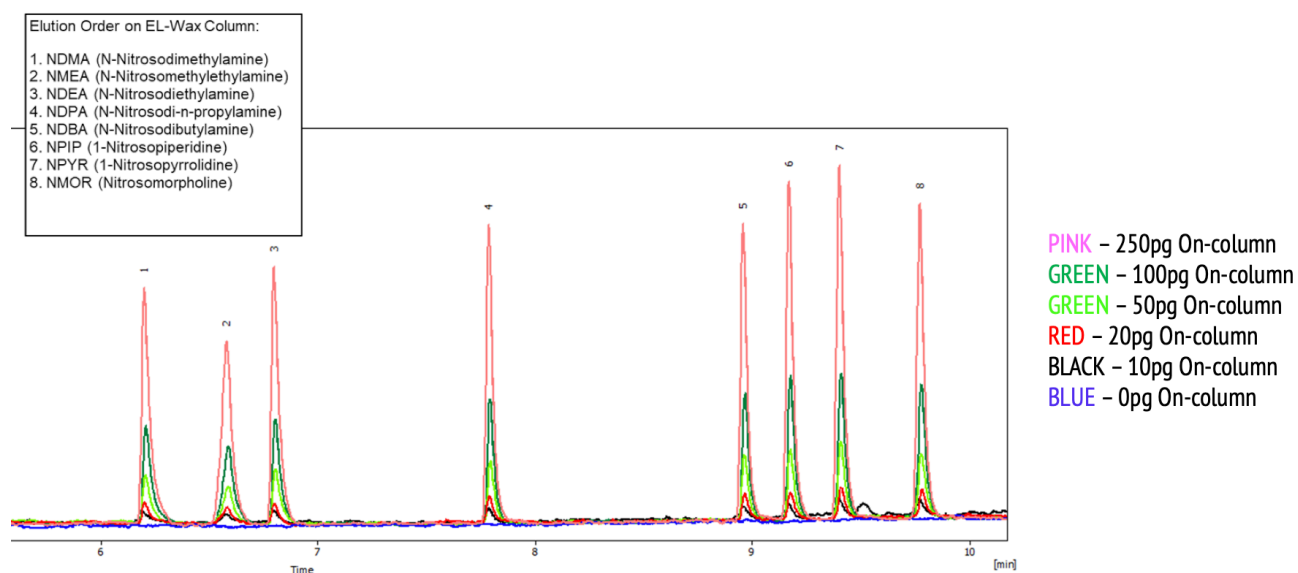
These calculations ensure the analysis aligns with the limits of detection (LOD) for each nitrosamine, with a daily exposure limit of 96ng or greater, and the maximum prescribed dosage.

Analytical Method

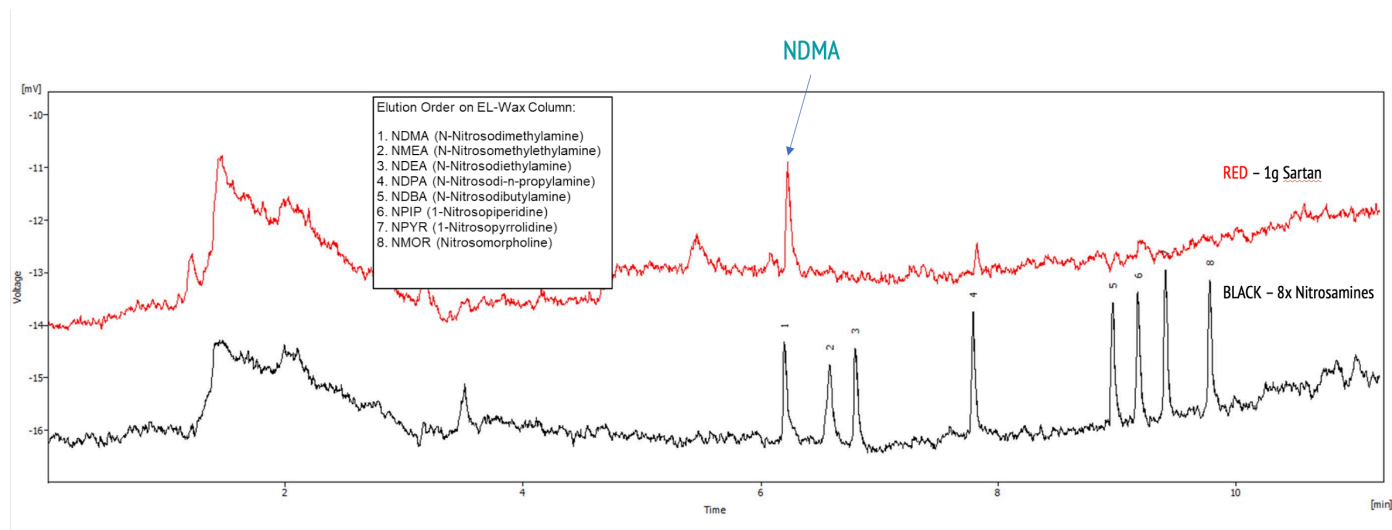
GC-TEA Calibration Curves



Calibration: 10pg on-column is 0.5µL injection of a 20ng/mL standard (20ppb per component) Signal:Noise – 5:1 on smallest peak



1g of a Sartan was extracted with 5mL methanol. 0.5µL splitless injection



Results

The above chromatogram is 100mg of a sartan with 900mg of excipient. It is clear that NDMA is present, but the area is less than the area of 40pg, so this tablet meets acceptance criteria for NDMA.

Conclusion

The GC-TEA system provides a sensitive means of quantitating real life samples to demonstrate regulatory compliance for the presence of specific nitrosamines in pharmaceutical samples.

Product Information

The part numbers listed below include all the components required to integrate the Thermal Energy Analyzer (TEA) with your existing Gas Chromatography (GC) system.

PN: 32000810 - TEA 810 - 230V50Hz

PN: 32020300 - 810 Pyrolyser Interface Kit

PN: 32001060 - 230V Ozone Destroyer (for TEA)

PN: 32020200 - NCDSi Dry Scroll Pump w/ Silencer

If you do not currently have a GC system and require one, we recommend our 200 Series GC. For more information about this GC solution, please visit <https://www.ellutia.com/200-series-gas-chromatograph>



To learn more about Ellutia's TEA, please visit:
<https://www.ellutia.com/800-series-tea-detector>

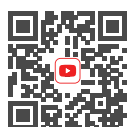


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