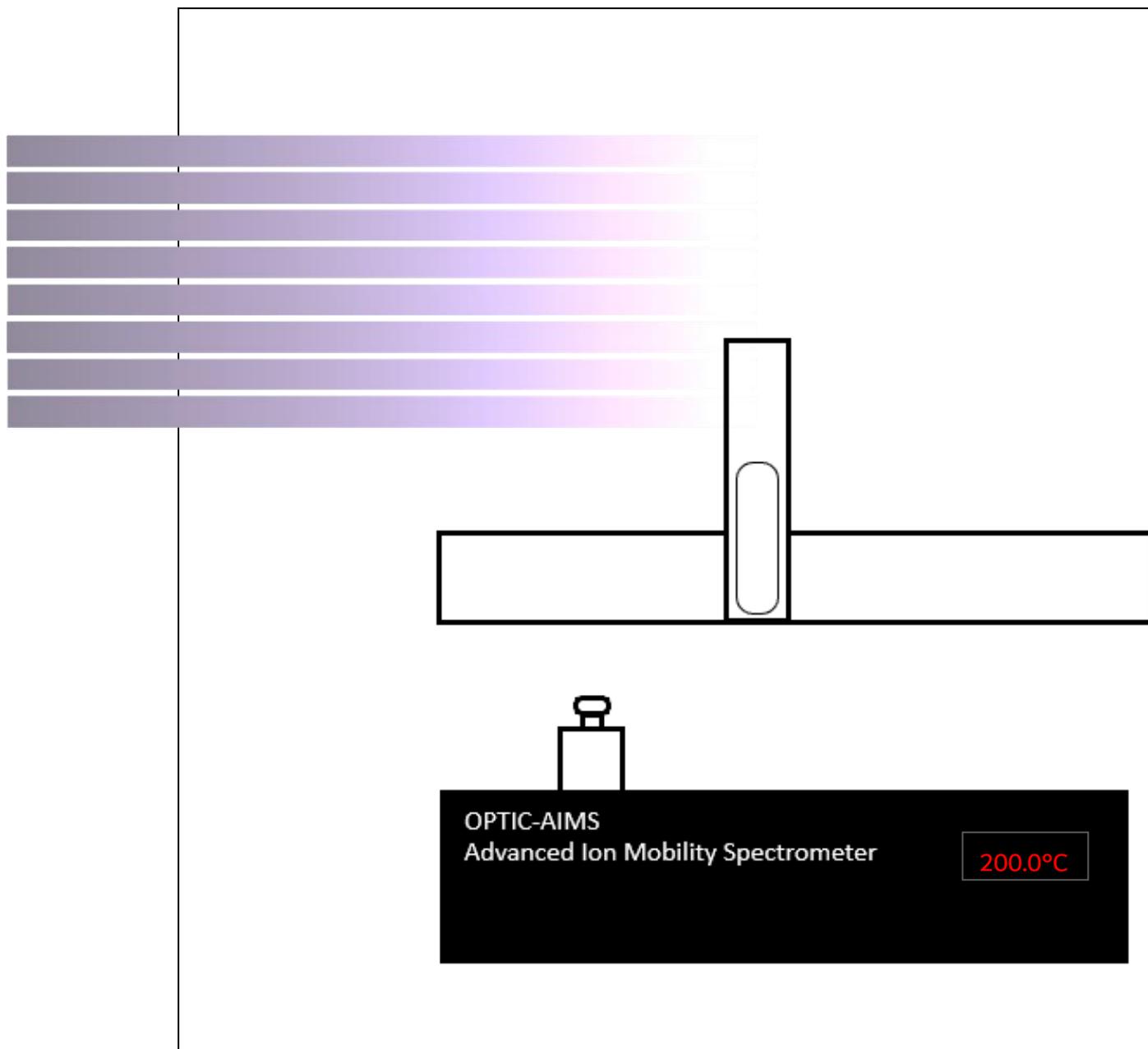


Clopidogrel: Cleaning Validation using OPTIC-IMS



Keywords: OPTIC, IMS, AIMS, Clopidogrel

Introduction

Cleaning validation is a vital step in the drug production process. It is to ensure that no cross-contamination occurs while switching between different products in a piece of equipment. Standard cleaning validation procedures are based on checking the cleanliness using liquid chromatography (LC). In average, it takes approx. 30 minutes and a significant amount of organic solvent before the production process is resumed into a next run assuming that the validation test has passed.

In this study it is shown that the cleaning cycle can be significantly reduced when using a fast measurement technique. The cleaning examination is performed using Clopidogrel as a sample drug.

Analytical conditions:

Analyzer:	OPTIC-AIMS, GL Sciences B.V. and MaSaTech s.r.o.
Transfer Line:	Fused Deactivated Silica, 0.25mm x 0.1 m
Temperature transfer line:	200°C
Injection mode:	OPTIC Expert mode
Sample volume:	1 µL sample
Inlet temperature program:	50°C → 60.0 °C/sec → 400°C
Column Flow:	20.0 mL/min conditioned Air
Venting:	75 mL/min conditioned Air, 6 sec
Drift tube temperature:	180°C
Drift Flow:	900 mL/min conditioned Air
Analysis Time:	150 s (including cool down time)

Sample Preparation:

The samples were taken from a reaction chamber that was used to produce Clopidogrel. A swab sample was prepared by wiping the chamber horizontally on one side of the swab. Each swab sample was then placed into a 20 mL vial containing 10 mL of Methanol. The vial was shaken for 2 minutes afterwards. 1 µL of the extract was injected into the OPTIC-AIMS.

Peak discovery:

Step 1: 1 μL injection of 0,7 $\mu\text{g}/\text{mL}$ Clopidogrel in Methanol into the OPTIC-AIMS.

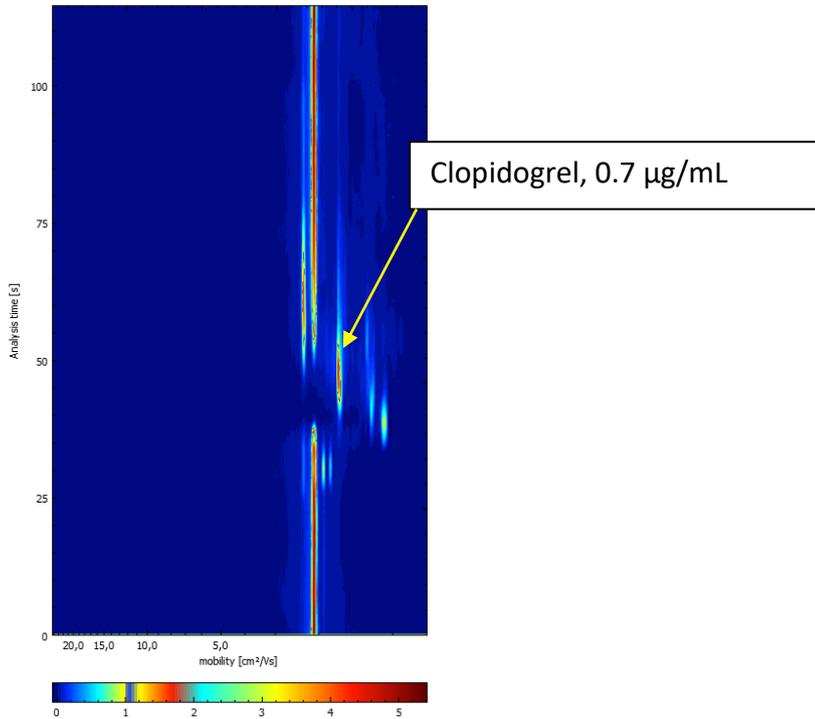


Figure 1. Plasmagram of 1 μL injection, 0.7 $\mu\text{g}/\text{mL}$ Clopidogrel in Methanol.

Step 2: Swabbing the reaction chamber after cleaning it with clean air.

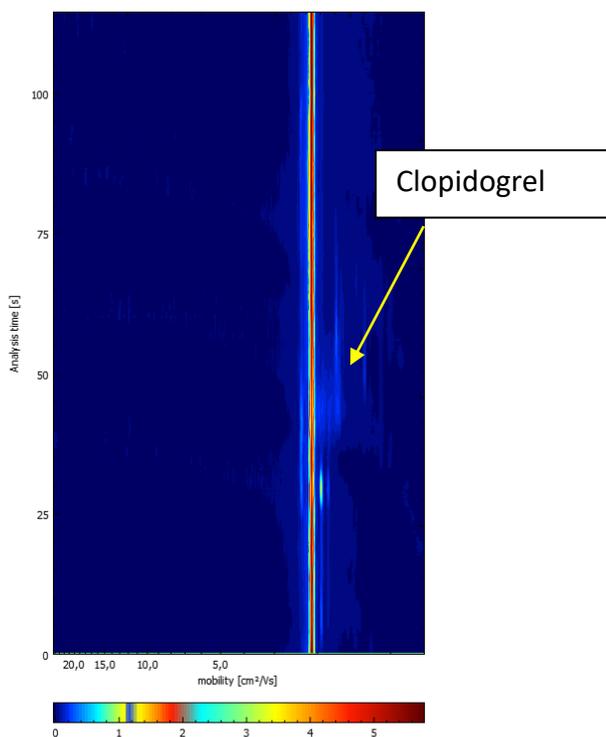
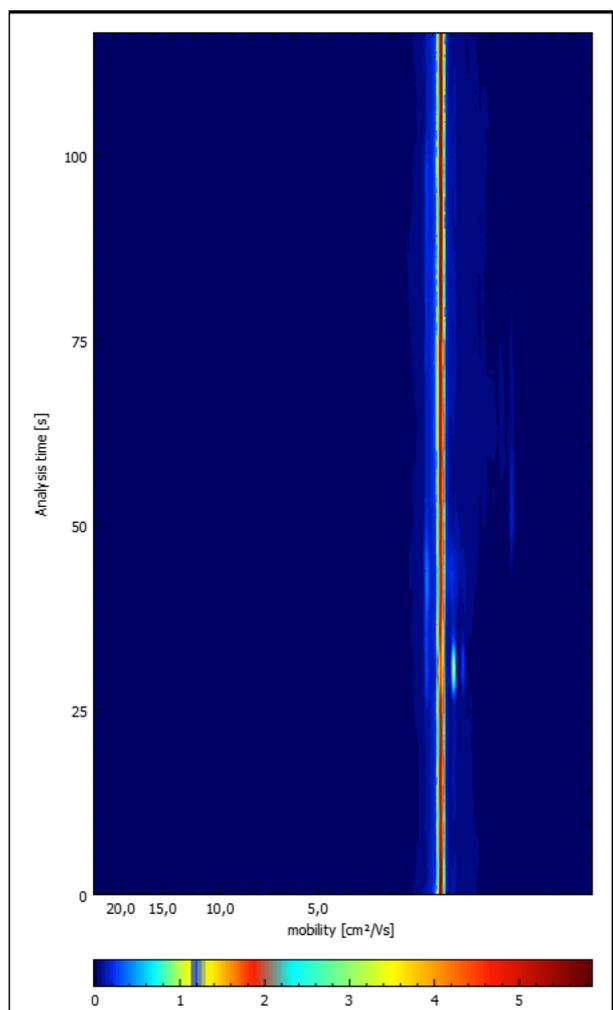


Figure 2. Plasmagram of 1 μL injection, a sample swab is rinsed in 10 mL of Methanol

Step 3: Swabbing the reaction chamber after wet cleaning.



Picture 3. Plasmagram of 1 μ L injection, a sample swab is rinsed in 10 mL of Methanol

Conclusions:

As it is seen from the plasmagrams, the OPTIC-AIMS analyzer is very much capable of detecting low concentrations of Clopidogrel. The compound is clearly visible before the wet cleaning. After the wet cleaning, the Clopidogrel is not detected. In accordance with the existing regulation, it is not permitted to have more than 0.7 ng/ μ L of Clopidogrel which is equivalent to 7 μ g/swab rinsed with 10 mL of solvent.

The OPTIC-AIMS system runs on conditioned (dry and cleaned) air. The analysis time is within 3 minutes. A low amounts of solvent (Methanol) is used for the sample preparation. At the same time, if an LC system is used for the cleaning validation, it consumes about 500 liter of solvent per year for the mobile phase if flow of 1 mL/min is maintained.

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