

# APPLICATION OF THE AGILENT AUTOMATED PURIFICATION SOFTWARE IN HIGH-THROUGHPUT PREPARATIVE HPLC-MS PURIFICATION WORKFLOW OF LIBRARIES WITHIN THE EUROPEAN LEAD FACTORY

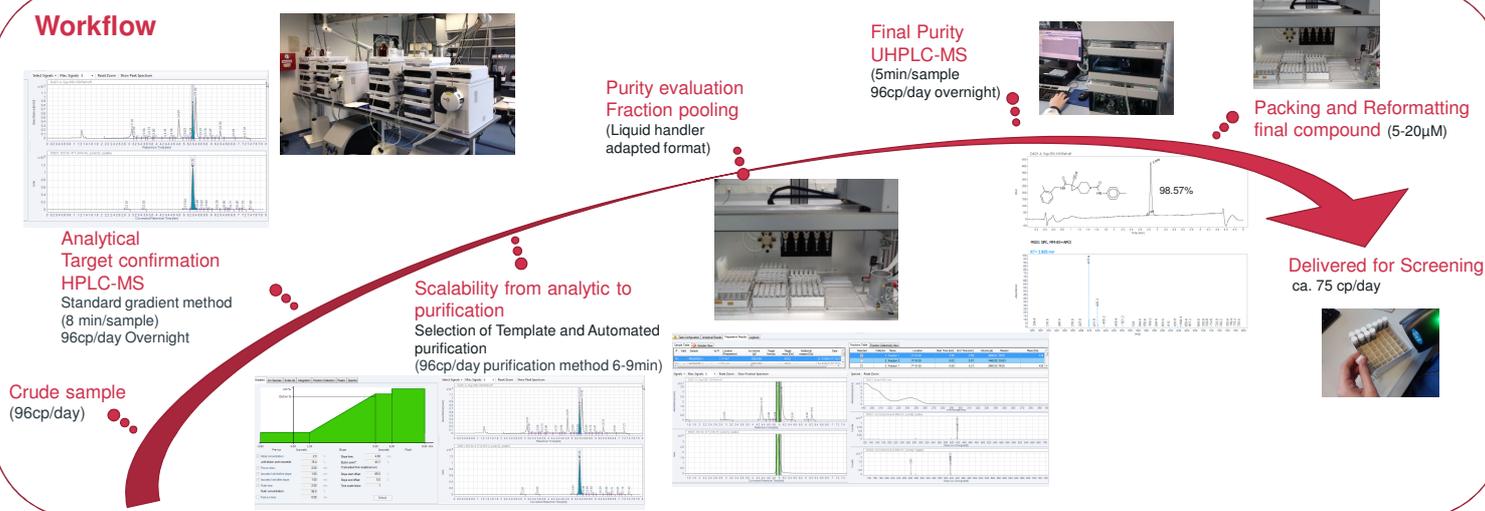
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## Introduction

The European Lead Factory is a collaborative public-private partnership established in 2013 aiming to deliver over 500 000 innovative drug discovery starting points in order to enhance the chances to find new valuable lead candidates that could result in the development of novel treatment options for patients. Taros Chemicals, a privately owned CRO company, is contributing with over 10 000 compounds per year into the Joint European Compound Collection (JECL). Within this poster we present a user friendly and highly efficient purification workflow based on Agilent OpenLAB CDS Automated Purification Software. The software has been developed by Agilent Technologies in a close collaborative project with Taros creating automated purification workflows based on reversed phase high performance liquid chromatography (HPLC) and mass spectrometry (MS). The system is suitable for a smart combination of UV- and mass-based fraction triggering and the automated transfer of data between each single process streamlining the workflow for highest productivity as the purification of crude products is usually the most time consuming part of organic compound preparation.

## Workflow



## Results and Discussion

**Polar Broad Peaks Separation**

**Low UV absorbance Purification**

**Library TC1321**  
(Underrepresented Monospirocycles library: 84% compounds sp<sup>3</sup> 0.6-0.8).

Challenges solved:

- Low UV absorbance compounds purified (35% of total library).
- Final diversification point: 5 types of chemistry in 3 different spatial positions (sulfonylation, amide coupling, acylation, reductive amination and urea formation).
- Difficult separations also successfully accomplished.
- Purification Methods between 6-9 min without decreasing the separation.

Results in Numbers:

- Purification success 80%.
- Median final purity 99%.
- Number of successfully synthesized and delivered compounds: 1478.
- Total time of purification: 20 days.

**Difficult samples Separation**

## Experimental

Analytical: UHPLC Agilent 1260 Infinity LC/MS System: 1260 Infinity Binary Pump (G4220A), 1260 Infinity Auto Sampler (G4226A), 1260 Infinity Thermostated Column Compartment (G1316A), 1260 Infinity Diode Array detector (G1315C) with the Standard flow cell, Agilent 6120 Quadrupole Mass spectrometer (G6120B). Preparative: Agilent 1260 Infinity preparative scale LC/MS Automated Purification System: 1260 Infinity Auto Sampler (G2258A), 1260 Infinity Preparative Pumps (G1361A), 1260 Infinity Diode Array detector (G1315D) with the standard flow cell, Agilent 1260 Infinity Fraction Collector PS (G1364B), Agilent 6120 Quadrupole Mass spectrometer (G6120B)

Columns: Waters ACQUITY UPLC@BEH C18, 2.1x50mm, 1.7µm, VanGuardTM Pre-Column 2.1x50mm; Waters XBridge® C18, 4.6x100mm, 3.5 µm, XBridge® C18, 3.5µm 4.6x20mm Guard Cartridge; Waters XBridge® C18, 19x100mm, 35µm, XBridge® C18, 5µm 19x10mm Guard Cartridge

Software: Agilent OpenLAB CDS ChemStation Edition for LC/MS, Rev. C.01.07 [11], Agilent Automated Purification Software Add-On, Rev. A.01.03 [42]

Solvents and samples, Purification mixture for analytical and preparative runs: drug-like samples, Solvent A: Water (HPLC-Grade) + 0.1% Formic Acid, Solvent B: Acetonitrile (HPLC-Grade) + 0.1% Formic Acid

## Conclusions

- A successful automated workflow has been established in the purification of libraries.
- 25% time saving by preselection of the crudes containing target compound.
- 15% time saving by the use of Purification templates with the purification software from Agilent that allows the purification of sequences of until 48 compounds. Semiautomatic Method Development.
- 1478 compounds have been delivered. Global purification success rate 80%. With a median purity of 99%.
- Purification time was reduced in a 30%. Solvent costs were reduced in a 40%.

