

A Highly Productive Semi-Automated High Throughput Purification Process

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Facts & Figures

Start date:	01/01/2013
End date:	31/05/2018
Contributions	
IMI funding:	79 999 157 €
EFPIA in kind:	91 657 070 €
Other:::	24 922 388 €
Total Cost:	196 578 615 €
Project website:	www.europeanleadfactory.eu
Social media:	
	de.linkedin.com/company/european-lead-factory
	twitter.com/euleadfactory?lang=de

Challenge

The European Lead Factory was a collaborative public-private partnership established in 2013 aimed to deliver over 200,000 innovative drug discovery starting points in order to enhance the chances to find new valuable lead candidates for the development of novel treatment options for patients. Taros Chemicals, a privately owned CRO company, has contributed with over 40,000 compounds to the Joint European Compound Collection (JECL). One of the challenges that was successfully addressed by Taros was the development of an efficient purification workflow in order to deliver the high number of final compounds. On this poster, we present a user friendly and highly efficient purification workflow based on Agilent OpenLAB CDS Automated Purification Software.

Approach & Methodology

The software has been developed by Agilent Technologies in a close collaborative project with Taros creating automated purification workflows based on mass directed reversed phase high performance liquid chromatography (HPLC/MS). The system is suitable for a smart combination of UV- and mass-based fraction triggering and the automated transfer of data between all steps of the process.

Impact & Take Home Message

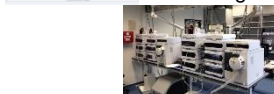
The primary goal of ELF was to deliver hit compounds that in turn can be translated into patents and drug candidates with the ultimate goal to improve patients' lives. ELF is the perfect instrument to address this challenge, through providing the early drug discovery community with the resources required to identify and better potential drug candidates with the potential to move faster into the clinic.

Moreover, the project has allowed us to set up an efficient workflow for the entire process of screening library production, improving largely the throughput by increasing the level of automation.

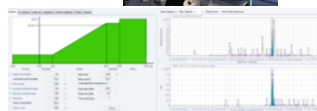
Crude sample
(96 cpds/day)



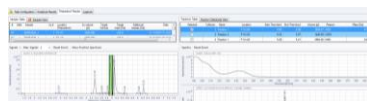
Analytical HPLC-MS
Target cpd confirmation
Standard gradient (8
min/sample) 96 cpds/day
overnight



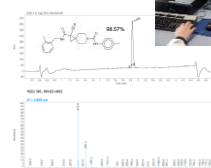
Scalability from
analytic to purification
Selection of template and
automated purification
(method 6-9 min
96 cpds/day purification)



Purity evaluation
& fraction pooling
(Liquid handler
adapted format)



Final purity
uPLC-MS
(5 min/sample
96 cpds/day overnight)



Packing and reformatting
final compound
(5-20 µM)



Delivered for screening
(ca 70 cpds/day)

Results

68 libraries have been synthesized and purified yielding >40,000 compounds. The workflow developed allowed the continuous purification of final compounds having both, low and high UV absorbance, and a wide range of polarity.

Results in numbers:

Purification methods were set up and optimized to short running times of 6-9 min without decreasing the separation, allowing a high throughput purification.

Purification success: > 70 %
Final purity: > 90 %
Average number of purification/day: 96 cpds
Average time of purification/library: 2-3 weeks
Number of delivered compounds: >40,000

Value of IMI Collaboration

Regular communications within the consortium allowed us to get involved into the process of screening library selection and to learn about the achievements in the production process. Moreover, a close collaboration with academic groups at the TU Dortmund and Max-Plank Institute contributed to the design and selection of new chemical entities.