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VRIJE UNIVERSITEIT BRUSSEL

PhD in Pharmaceutical Sciences
2017-2018

INVITATION to the Public defence of

Charlene MUSCAT GALEA

To obtain the academic degree of **'DOCTOR IN PHARMACEUTICAL SCIENCES'**

Drug impurity profiling in supercritical fluid chromatography – Understanding the influence of the parameters required for method development.

Wednesday 13 December 2017
Auditorium **Piet Brouwer**, 17:00
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

How to reach the campus Jette:
http://www.vub.ac.be/english/infoabout/campuses

Summary of the dissertation

Drug impurity profiling is regulated by stringent drug registration procedures established by regulatory authorities. Currently high performance liquid chromatography (HPLC) is the mainstay technique used in the pharmaceutical industry for this purpose. However, the quest for complementary, faster, cheaper, greener and more efficient techniques will always be strong. Supercritical fluid chromatography (SFC) fulfils these needs and because of the recent instrumental improvements, it is now being explored for drug impurity profiling.

The aim of this thesis was to investigate different experimental parameters, mainly the stationary phase, modifier composition, column temperature and back-pressure, and their effect on separation in SFC, within the context of method development for drug impurity profiling. Initially a database of stationary phases was characterized using retention profiles of a representative set of pharmaceutical compounds. Several chemometric techniques and an adapted linear solvation energy relationship (LSER) model were used to cluster the columns in sub-groups of similar properties and subsequently select a small set of dissimilar phase to be used for further method development. In the second phase, the influence of binary organic solvent blends as modifier on the retention and separation of achiral components was investigated. This was followed by a method optimization study to fine-tune the column temperature and back-pressure using a response surface approach. Finally the complete methodology was tested on a pharmaceutical drug and its impurities from the industry. The main knowledge obtained from the different phases of the thesis was brought together in a generic strategy.

Curriculum Vitae

Charlene Muscat Galea was born on 24th May 1989 in Malta. In 2011 she came to the Vrije Universitiet Brussel (VUB) as an exchange student to work on a project comparing different response surface designs to optimize a high performance liquid chromatography (HPLC) separation of a β-blocker mixture under the supervision of Prof. Dr. Bieke Dejaegher. She obtained her pharmacist degree with distinction from the University of Malta in 2013. After that she moved to Brussels to start her PhD in Pharmaceutical Sciences, centred on method development for drug impurity profiling in supercritical fluid chromatography (SFC), at the Department of Analytical Chemistry, Applied Chemometrics and Molecular Modelling. She was working under the supervision of Prof. Dr. Yvan Vander Heyden and Prof. Dr. Debby Mangelings.

The results obtained during her doctoral research work were presented at several national and international scientific conferences as oral and poster presentations. Charlene's work has resulted in six scientific publications in international peer-reviewed journals, all of which as first author. In addition, she has worked on four book chapters. Charlene was also co-promoter of five master theses and assisted in the analytical chemistry practical courses of the 3rd year Bachelor and 1st year Master pharmacy students.