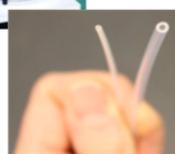


Continuous-flow process for the preparation of methylphenidate hydrochloride

Methylphenidate hydrochloride, a central nervous system stimulant, is the active ingredient of medications such as Concerta, Ritalin, Metadate, Methylin,... that are amongst the most widely prescribed stimulant medications to treat attention deficit hyperactivity disorder (ADHD) and narcolepsy (2,4 billion doses per year in 2013). The methods used for the preparation of this molecule are mainly based on stepwise macroscopic batch processes which come with various shortcomings (poor mixing...) ultimately accounting for low productivity, quality deficiency and poor flexibility. Besides, an increasing chemical risk is associated with classical large scale, stepwise batch processes, in particular when highly reactive species or hazardous/explosive intermediates are involved.

Description

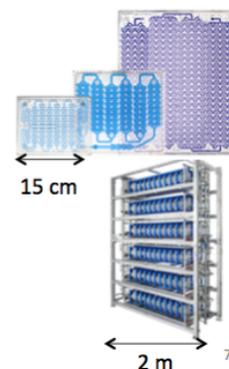
The patented technology relates to a scalable, safe and intensified **continuous-flow process in micro/mesofluidic reactors for the production of methylphenidate hydrochloride**. Besides, the patented invention provides various methods for synthesizing some specific pharmaceutically active species (reaction intermediates of methylphenidate synthesis), by using continuous-flow conditions with a drastically improved efficiency by comparison to the batch procedures.



Channel \varnothing : up to 800 μm
 V_{int} : μL - mL

Microreactor (typ. 250 μL V_{int})
 -Explore and develop chemistry
 -Optimize reaction (R&D)

Channel \varnothing : < 1 mm
 V_{int} : > 1 mL



Mesoreactors (typ. 10 mL V_{int})
 -Pilot and production

Advantages

- overcomes the shortcomings of the batch processes : better mixing and heat transfer, accurate control on the reaction conditions, **improved yield production** and obtention of a product with a constant quality and purity profile
- safer process
- faster process (few minutes instead of few hours)
- cleaner process (minimal footprint)

Potential Applications

The patented technology consists in an alternate more cost effective process to produce methylphenidate hydrochloride, or to synthesize any of its reaction intermediates.

Development stage

Continuous-flow conditions of the whole methylphenidate hydrochloride synthesis process were optimized at microfluidic scale in lab (production yield around 20 g / day scale).

One critical reaction step of the process was validated on a commercially available pilot mesoscale continuous-flow reactor enabling a productivity of 4.25 kg / day.

Patent Status

Pending : EP 16189458.9 A1

Research Team

This technology has been developed by Jean-Christophe Monbaliu's team, from the Center for Integrated Technology and Organic Synthesis (CiTOS) at the University of Liège (ULg).

The Center for Integrated Technology and Organic Synthesis is a multidisciplinary team with research interests around synthetic organic chemistry, with a particular focus on continuous flow processes for the synthesis of organic compounds of interest.

Jean-Christophe Monbaliu completed his PhD thesis at UCL (Belgium). After a first postdoctoral position at the University of Ghent in Belgium (2008-2010), he joined the Center for Heterocyclic Compounds at the University of Florida in Gainesville (USA). During these postdoctoral fellowships, he studied chemical engineering, specialising in the application of microfluidics to organic chemistry. In 2012, he was appointed at the Massachusetts Institute of Technology (MIT) in Cambridge, MA. The team's goal was to develop a portable drug production unit, giving rise to a key article in Science. In 2013, he came back to Belgium, settled at ULg and created the Center for Integrated Technology and Organic Synthesis.

Opportunities

Research collaboration and/or license agreement

Contact

Helene Sabatel
h.sabatel@ulg.ac.be
Tel : +32 4 349 85 29

ITF file n° 2016-06

Continuous-flow process for the preparation of methylphenidate hydrochloride

- I am interested in learning more about the general aspects of this technology. Please contact me.

The best time to reach me is: _____

- I would like an electronic version of this technology.
- I would like to learn more about the specifics of this technology and would be willing to complete a Confidential Disclosure Form in order to discuss it further.
- I am not interested in this technology because: _____

- I am not interested in this technology but would be interested in learning more about (please specify): _____

Name: _____

Title: _____

Company: _____

Address: _____

Phone: _____ Fax: _____

E-mail: _____

Please send it back to Gesval

info@gesval.be - Fax : + 32 4 349 85 20