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Continuous Flow Synthesis of Lorazepam

A high-throughput, five-step continuous flow synthesis method for Lorazepam delivers high purity (>99%) and yield, offering accelerated scale-up and reliable, continuous drug production using safer, sustainable reagents.

Researchers at Purdue University have developed a method for continuous flow microfluidic synthesis of benzodiazepines such as Lorazepam. Lorazepam is a commonly used sedative and is classified as an 'Essential Medicine' by the World Health Organization. However, the drug is subject to periodic shortages as the U.S. lacks domestic manufacturing capability. What's more, the drug is produced batchwise, a process that suffers from process irreproducibility issues, inability to scale readily and large time consumption. The Purdue researchers established a method--the reagents, catalysts, solvents, process conditions (temperature, pressure, flow rate, residence time), and equipment--for high throughput, continuous synthesis of Lorazepam at high yield and purity in a single reactor. The researchers propose a five-step process with a total residence time of 72.5 minutes.

Related Publication: Development of a Continuous Flow Synthesis of Lorazepam. Shruti A. Biyani, Corryn Lytle, Seok-Hee Hyun, Michael A. McGuire, Ranya Pendyala, and David H. Thompson. Organic Process Research & Development 2022 26 (9), 2715-2727. DOI: 10.1021/acs.oprd.2c00184

Technology Validation: A step-by-step comparison of batch and continuous flow synthesis of Lorazepam was done, and it was found that the five-step continuous flow synthesis had a significantly reduced total synthesis time, improved yield of product at each step and minimized impurities, and it avoided purification methods such as column chromatography and used milder, safer, and sustainable reagents and solvents in each step. Under evaluation with ultra-pressure liquid chromatography (UPLC), the Lorazepam synthesized by the researchers' continuous flow process was shown to be over 99% pure.

Advantages:

- Continuous production

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Category
Chemicals & Advanced Materials/Materials Processing & Manufacturing Technologies
Pharmaceuticals/Pharmaceutical Manufacturing & Methods

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View online

- Accelerated scale-up process

- > 99% purity

- High yield synthesis

- Use of non-toxic, sustainable reagents

Applications:

- Lorazepam synthesis

TRL: 3

Intellectual Property:

Provisional-Gov. Funding, 2022-08-08, United States | PCT-Gov. Funding, 2023-08-07, WO | NATL-Patent, 2025-02-07, United States

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