An entirely new way of manufacturing pharmaceutical and other valuable chemicals

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An understanding-based tool could help process development teams to decide whether switching from batch reactor system to continuous product manufacturing makes techno-economic sense. Credit: A*STAR Institute of Chemical and Engineering Sciences

Historically, pharmaceutical industries have relied on novel medications

to meet profit targets; however in today's competitive markets, the huge expenditures associated with drug development now challenge this approach. An international team led by A*STAR researchers show how manufacturers can make rapid decisions about switching to alternative drug manufacturing procedures with promising economic prospects.

High-value chemicals are traditionally made through 'batch processing'; where inputs such as raw materials and energy are combined in a single reactor until the desired output is obtained. While this approach is simple, it can only be performed in a sequential manner. So if demand for a drug suddenly increases—combating an emerging strain of influenza, for instance—such step-by-step operations cannot cope with the production scale-up required.

Soo Khean Teoh from the Institute of Chemical and Engineering Sciences at A*STAR and her co-workers have developed a methodology to assess the feasibility of switching from batch to 'continuous' processing, where all stages of chemical reactions occur simultaneously: flowable reagents are constantly fed into reactor, and likewise, products are extracted nonstop.

With continuous processing, operations are quicker, more energy-efficient, and use smaller installation facilities than batch techniques. Yet most chemical producers are hesitant to implement continuous systems, unless they see clear technical and economic benefits.

"The biggest challenge is that there is no 'one-size-fits-all' solution for changing from batch to continuous methods, because of the complex and varied chemistries involved," explains Teoh. "We had to devise a method which guides users to understand the process in question, brainstorm about potential benefits, and help them come to swift decisions."

The researchers' method initially screens chemical processes to uncover

key business requirements and potential pitfalls, such as sticky reagents, with simple yes/no/maybe evaluations. Successful candidates are then broken down into a flow chart analysis that identifies factors such as possible equipment, control schemes, and plant configurations. If the analysis makes economic sense, a final stage of process execution is put into place.

Liquid-phase reactions that proceed quickly and emit or absorb large quantities of energy proved to be particularly favorable for continuous processing. For example, the team demonstrated that the Reformatsky reaction—an organozinc-catalyzed reaction that frequently overheats with batch processing—could profit enormously from a continuous approach.

"Our methodology makes understanding the process much clearer, especially to the chemists and engineers dealing with the synthesis," says Teoh. "It makes it easier to decide to proceed or to kill the idea, minimizing wasted effort."

More information: Soo Khean Teoh et al. Practical Assessment Methodology for Converting Fine Chemicals Processes from Batch to Continuous, *Organic Process Research & Development* (2016). DOI: 10.1021/acs.oprd.5b00001

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