Concentrating complex drug factories into a single small reactor, inspired by the cell

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The production method for many drugs and chemicals is laborious, with a separate reactor for each chemical reaction. A research consortium led by TU/e professor Volker Hessel is taking a completely different approach. Within biological cells chains of reactions occur faultlessly next to and through each other. The researchers want to imitate this and so enable chains of reactions to occur simultaneously, within a single reactor. The goal is to make huge savings in terms of the production and development costs of drugs and create new opportunities for personalized drugs. The research, which has a four-million euro EU subsidy, begins in January.

The production of drugs and chemicals usually requires several chemical reactions to arrive at the end product. Current practice is for these reactions to occur separately in their own reactor, in which the temperature, pressure and solvent are all adjusted to the specific reaction. Moreover, the reactor tends to be a batch reactor, which means that a large amount of raw materials goes in, is slowly processed and then exits, usually hours or days later. This is really laborious and time-consuming. For each reaction the mixture has to be brought to the right temperature and then cooled again later. And between each stage of the process, the desired semi-product has to be separated and purified from unwanted bi-products.

But there is another way believes a collective group of researchers from TU Eindhoven, TU Delft and various other universities abroad. They are inspired by the biological cell, a tiny space in which nature succeeds in

enabling many different chemical reaction chains (cascades) to take place, at the same pressure and temperature and in the same solvent (water). And constantly, which means fast. Cells do this using enzymes, substances that give the reactions a helping hand. The researchers want to be able to make drugs in the same way in small chemical reactors that operate constantly.

The potential benefits are manifold. The whole process runs much faster, requires much less energy and space, results in less waste and no environmentally harmful solvents are needed. It is also possible to work with much smaller quantities, something that favors the production of personalized drugs, for example. Much less, and smaller, equipment is needed, too. The researchers estimate the savings generated by the introduction of the technology they will be developing to run into tens of billions worldwide. As test cases for this new approach, they will be using four very common existing drugs (analgesic cannabinoids, the gallstone drug ursodiol, the anti-hypertensive medication Valsartan and the cancer treatment drug Capecitabine).

The researchers will have to overcome a number of significant hurdles along the way. If the different chemical reactions are to take place concurrently, they are not allowed to influence each other. The researchers will develop a range of methods to enable the requisite isolation for the different reaction stages by creating chemical or physical compartments, taking inspiration from the way nature does this. They also want to investigate whether they can only combine reactions that do not influence each other – whereby no isolation would be required anymore. There will be special focus on modern process control assisted by the Chemical Internet of Things, which will be a much more complex matter than in the classical step-by-step method. The ultimate goal of the researchers and one awarded high-tech SME is to use the new insights to deliver a ready-made new production technology available on the market.

TU Eindhoven is the biggest participant in the project known as ONE-FLOW (Catalyst cascade reactions in ONE-FLOW within a compartmentalized, green-solvent 'digital synthesis machinery' – end-to-end green process design for pharmaceuticals), and besides Volker Hessel includes from TU/e professors Kitty Nijmeijer and Jan van Hest along with Dr. Tim Noël, all from the department of Chemical Engineering. Other partners are TU Delft, TU Graz, Universität Bielefeld, Centre National de la Recherche Scientifique, University of Cambridge, the University of Hull and the Austrian company Microinnova Engineering. The project partners have been given a subsidy worth nearly 4 million euros from the EU's FET-Open program for 'radical new technologies'.

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