New method is a significant step towards greener pharmaceutical industry

October 27 2020

Professor at TalTech's Division of Chemistry Riina Aav Credit: TalTech

The rapid changes in the chemical industry are connected on one hand with the depletion of natural resources and deepening of environmental concerns, and on the other hand with the growth of environmental awareness. Green, environmentally friendly chemistry is playing an increasingly important role in the sustainable chemical industry.

The TalTech Supramolecular Chemistry Group led by Professor Riina Aav published a research article on the applications of mechanochemistry titled "Mechanochemical Synthesis of Amides with Uronium-Based Coupling Reagents: A Method for Hexa-amidation of Biotin[6]uril" in the journal *ACS Sustainable Chemistry and Engineering*.

Mechanochemistry is a branch of chemistry that studies the effects induced by mechanical action on chemical reactions. Since these reactions take place efficiently in the solid-state phase and do not require the use of solvents that generate toxic residues, it is becoming an increasingly important branch of chemistry, especially in the field of green and sustainable technology.

One of the authors of the article, TalTech Professor of Chemistry Riina Aav says, "Our Supramolecular Chemistry research group is currently one of the most active research groups in this field in Estonia, investigating in depth how to expand the possible applications of the mechanochemical method in the chemicals industry. As chemists, we see this method in particular as a good solution for environmentally friendly synthesis. This means that it is now possible to produce chemicals much faster and completely residue-free."

Twenty five per cent of pharmaceuticals produced in the chemical industry contain an amide bond. Such pharmaceuticals include e.g. drugs for the treatment of cardiovascular diseases (atorvastatin or Lipitor), analgesics (Ibuprofen analogs), antibiotics (penicillin and chloramphenicol or Oftan Akvakol), as well as cancer drugs (methotrexate and, inter alia therapeutic peptides such as carfilzomib (KYPROLIS)). Until now, such drugs have conventionally been produced in the chemical industry using solvents. A mechanochemical process involves grinding of chemical substances without the need to use solvents. This means, however, that no toxic waste characteristic of solvent-based production is generated, and in addition, the whole process

can take place tens of times faster (e.g. the required active ingredient is created within an hour, whereas the analogous solvent-based reaction requires 24-hours).

"I would like to point out that we were able to replace the organic catalysts used so far with an inorganic one to achieve the result, because dissolution of components is not necessary in mechanochemical synthesis. This further reduced our carbon footprint. We also studied the mechanism of the mechanochemical process, and the results show that the formation pathways of amides or peptides, which are essential for the manufacture of pharmaceutical products, are similar to the ones involved in protein formation in our bodies. The mechanochemical method developed by us is much simpler—the necessary elements are ground and the product obtained is washed with water," a co-author and senior researcher Dzmitry Kananovich, says.

It is a faster and and much more environmentally friendly chemical process compared to the solvent-based method. In addition, this method can be used to produce new molecular receptors biotin[6]urils, which scientists plan to apply as "chemical noses" upon developing residue capturing molecular containers.

"The developed method is great news for chemical and pharmaceutical industry, who are interested in sustainable and residue-free chemical technology solutions not only in the production of medicines, but also food supplements, detergents and other products. Our research group is a member of the European Cooperation in Science and Technology action "Mechanochemistry for Sustainable Industry", which will hopefully ensure practical application of the mechanochemical methods in the chemical industry in the near future," Riina Aav says.

More information: Tatsiana Dalidovich et al, Mechanochemical Synthesis of Amides with Uronium-Based Coupling Reagents: A Method

for Hexa-amidation of Biotin[6]uril, *ACS Sustainable Chemistry & Engineering* (2020). DOI: 10.1021/acssuschemeng.0c05558

Provided by Estonian Research Council