 DOI: 10.33892/aph.2021.91.234-235

P-36

EPIPHARMA – From Cutting Edge Synthesis Technologies to Complete Preclinical Characterization

ISTVÁN MÁNDITY[1,2,3]; JÓZSEF MALÉTH[1,4]; BEÁTA MÁNDITYNÉ HUSZKA[1,3]; PETRA PALLAGI[1,4]; GÁBOR HELTOVICS[1]

[1] Epipharma Drug Development LLC., Szőregi Str. 38., H-6726 Szeged, Hungary
[2] Semmelweis University, Högyes Endre Str.7., H-1092, Budapest, Hungary
[3] Research Center for Natural Sciences, Magyar Tudósok krt. 2., H-1117, Budapest Hungary
[4] University of Szeged, Dugonics sqr. 13., H-6720, Szeged, Hungary

Correspondence: gheltovics@gmail.com

Keywords: *Synthesis, peptide, foldamer, ex vivo models, biomedical research,*

1. Introduction

The EPIPHARMA supports clients and partners in their peptide based drug development programs and provide an unparalleled laboratory research environment for characterizing, testing and evaluating new potential treatment approaches. From the chemical point of view a vide range of top of the line continuous -flow reactors are available not only for the synthesis of peptides but for building blocks and regular organic compounds too. The biomedical facility supports downstream preclinical characterization of the developed compound. The available techniques range from molecular biology and advanced microscopy to *ex vivo* and *in vivo* models. Flexible assay development is also part of the services.

3. Results

PAGEs and columns

Continuous flow (CF) approaches are of considerable current interest: highly efficient and selective reactions can be performed in CF reactors, constructed so as to possess pores and tubes in the active zone with diameters in the micro- or millimetre range. The surface to volume ratio in such microstructured devices is therefore orders of magnitudes higher than in conventional batch reactors. In consequence of this, micro- and mesoscale CF reactors offer a number of advantages over conventional batch technologies, such as faster heat and mass transfer, accurate control over the reaction temperature, a laminar flow profile, etc. These properties crucially influence the experimental set-up and the reaction outcome of a CF reaction. In contemporary flow technologies therefore the large-scale use of reagents and solvents is unnecessary and the most important reaction parameters, i.e. the flow rate, temperature and pressure can be adjusted and observed in a previously unprecedented way. The reaction outcome changes because of the faster mass transfer and considerably faster reactions can be carried out.

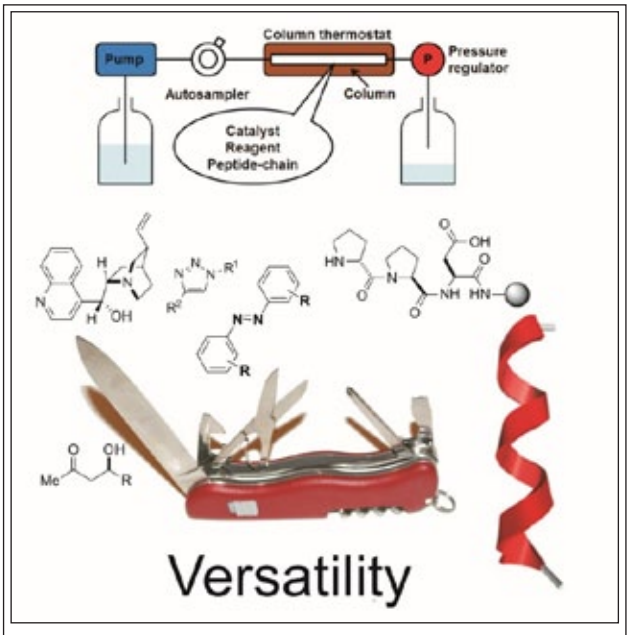

Figure 1 *General features of continuous-flow reactors available at EPIPHARMA*

Moreover, the more accurate temperature control and faster heat transfer result in more selective reactions, with higher yields of the desired product. This is in good accord with the first of the 12 principles of green chemistry defined by Anastas and Warner, which emphasizes that it is

easier to prevent waste formation than to handle or eliminate it. What is more, through the use of a pressure regulator, high-pressure and/or high-temperature reactions can be carried out. As a result, the reaction parameter space is considerably wider than those of conventional batch technologies, and this can be utilized through the experimental tuning of the CF reaction. Accurate residence time control can further broaden the versatility of CF processes, the availability of a wide range of applicable immobilized catalysts and reagents adds to the flexibility of CF techniques, and gaseous and dangerous reagents can be safely handled in CF devices. These features explain why CF reactions are currently becoming widespread in industrial drug synthesis and also the broad range of organic compounds available directly at EPIPHARMA.

4. Conclusions

EPIPHARMA combines cutting edge organic chemistry with advanced preclinical research capabilities. This unique combination enables rapid development of new compounds and powerful preclinical characterization, which can facilitate drug development programs.

5. Acknowledgements

The project is supported by the National Research, Development and Innovation Office (Grant No.: 2020-1.1.5-GYORSÍTÓSÁV-2021-00009).

References

1. *Mándity, I.M., Ötvös, S.B., Szöllösi, G., Fülöp F., Harnessing the versatility of continuous-flow processes: selective and efficient reactions, Chem. Rec., 16: 1018-1033 (2016).*
2. *Carino, G., Mathiowitz, E., Oral insulin delivery, Adv. Drug Del. Rev., 35: 249-257 (1999).*
3. *Elsayed, A., Al Remawi, M., Qinna, N., Farouk, A., Badwan, A., Formulation and characterization of an oily-based system for oral delivery of insulin, Eur. J. Pharm. Biopharm., 73: 269-279 (2009).*
4. *Badwan, A., Remawi, M., Qinna, N., Elsayed, Arafat, A., Melhim, M., Abu Hijleh, O., Idkaidek, N., Enhancement of oral bioavailability of insulin in humans, Neuroendocrinology Letters, 30: 101-105 (2009).*
5. *Molnár R, Madácsy T, Varga Á, Németh M, Katona X, Görög M, Molnár B, Fanczal J, Rakonczay Z Jr, Hegyi P, Pallagi P, Maléth J. Mouse pancreatic ductal organoid culture as a relevant model to study exocrine pancreatic ion secretion. Lab Invest. 2020 Jan;100(1):84-97.*
6. *Maléth J, et al. Alcohol disrupts levels and function of the cystic fibrosis transmembrane conductance regulator to promote development of pancreatitis. Gastroenterology. 2015 Feb;148(2):427-39.e16.*