Nanosystems as biomimetic interfaces: a new strategy to predict drug candidate biophysical profile

E. Fernandes[1]
S. Benfeito[2], F. Cagide[2], C. Fernandes[2], F. Borges[2] and M. Lúcio[1]

[1]*CFUM – Centre of Physics of University of Minho and Porto, Campus de Gualtar, Braga, Portugal*
[2]*CIQUP/Biochemistry and Chemistry Department, Faculty of Sciences, University of Porto, Porto, Portugal*

eduardabfer@gmail.com

Abstract

Drug screening based in drug candidate profiling is now widely viewed as an important bottleneck in the drug development process. [1]
Considering that in physiological environment there will be reciprocal interactions between drugs and biological interfaces, such as cell membranes or plasma proteins, and from those interactions different pharmacokinetic profiles can be achieved [1, 2], nanotechnology could be a powerful tool to design new mimetic models. Biomimetic systems as nanoscale models provide useful tools to mimic different physiological environments that ally the measurement of fundamental biophysical properties to the ADMET profiling (absorption, distribution, excretion and toxicity at the membrane level) of newly synthesized drugs. [3] The application of different biophysical techniques (derivative spectroscopy; quenching of steady-state and time-resolved fluorescence; quenching of intrinsic fluorescence of human serum albumin; synchronous fluorescence; dynamic and electrophoretic light scattering; differential scanning calorimetry and small and wide angle x-ray diffraction) in a high-throughput screening approach allowed to predict that a newly synthesized drug MIT3 [4] has an ubiquitous location at the membrane level, presenting good membrane permeability properties and a good distribution in the therapeutic target. However, it presented bioaccumulation in non-therapeutic targets and under prolonged exposure conditions, the MIT3 may cause membrane toxicity as concluded by impairment of membrane biophysical properties. Thus, all this gathered information is intended to give drug discovery researchers some tools to support decisions related to modifications of the drug chemical structure to improve drugs' properties and thus increase the probability of success in the process of drug discovery.

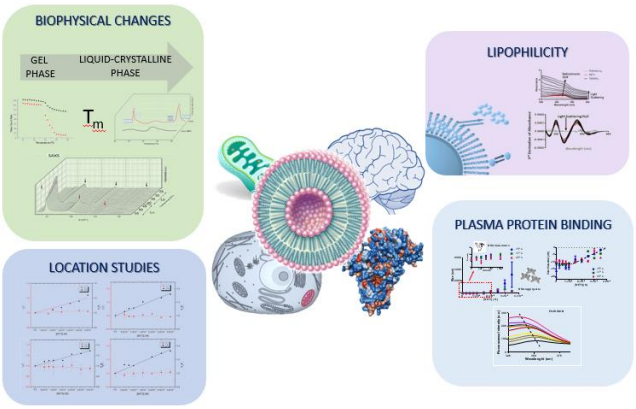

Figure 1: Representative summary image of the research developed

References

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