Bio-inspired models and biophysical studies applied in ADMET profiling

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Molecular interactions between cell membranes and drugs have a crucial effect on the pharmacokinetics (PK) and therapeutic efficacy of drugs [1]. These interactions determine the partitioning, position and orientation of drugs in membranes and thus play a significant role in the transport, distribution, accumulation and, eventually, in the therapeutic impact of drugs. In addition, drug-membrane interactions can also modify the biophysical properties of the membranes and therefore affect their functionality, which is responsible for the toxic effects of drugs at membrane level [2]. Molecular interactions between cell membranes and drugs are therefore important for the determination of the drug profile ADMET (absorption, distribution, metabolism, elimination and toxicity) that essentially determines the PK of drugs. Herein, we propose to illustrate how some biophysical techniques and bioinspired models may be used in the estimation of specific physicochemical main descriptors and in conjunction with silico models to forecast drug PK characteristics [2].
Interactions of drugs with mimetic models of biological interfaces include: (i) drug partitioning and thermodynamics aspects of drug distribution within membrane mimetic nanosystems studied by derivative spectrophotometry; (ii) drug effect on the biophysical properties of the membrane models studied by dynamic light scattering (DLS), fluorescence anisotropy, atomic force microscopy (AFM) and synchrotron small and wide angle X-ray scattering (SAXS and WAXS); (iii) drug molecular orientation within the lipid bilayer studied by steady-state, time-resolved fluorescence and computer simulations; (iv) drug binding to the blood carrier protein albumin and resulting conformational changes studied by the quenching of intrinsic protein fluorescence, derivative spectrophotometry and dynamic and electrophoretic light scattering (ELS) and (v) drug PK parameters (unbound drug fraction in plasma and tissues; volume of distribution and theoretical off-target distribution). The results obtained *in vitro* were compared with drugs biological effects *in vivo*.

FIGURE

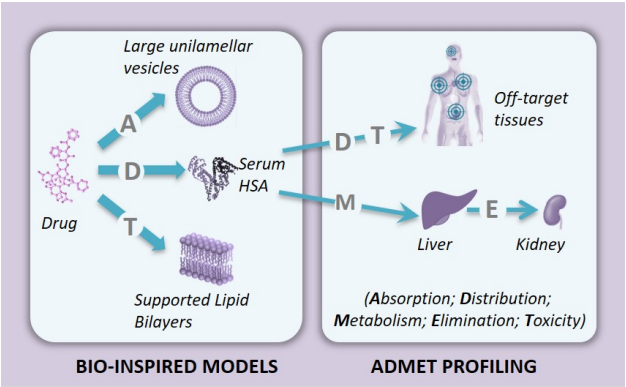

Figure 1: Bio-inspired models applied in ADMET profiling

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