Application of in silico classical drug discovery tools for peptide research

APPLICATION OF IN-SILICO "CLASSICAL" DRUG DISCOVERY TOOLS TO PEPTIDE RESEARCH

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The use of in-silico tools is well consolidated in the Drug Discovery process. A plethora of methods were developed to describe and predict the various steps of drugs action (e.g. ADME-TOX and pharmacodynamic events). These methods are traditionally focused on small organic molecules.

Very recently Pharma industry has expanded its interest into gene families such as peptidic GPCRs, protein kinases and proteases. Indeed other target classes, such as inhibition of protein–protein interactions, are requiring molecules. [1] Among them, peptides are becoming more and more interesting since they offer several advantages over small organic molecules and their known limits (e.g. poor stability) can be overcome. In the next future peptides and their homologous compounds (proteins and antibodies) are expected to be used in multiple pathologies, including allergy and asthma, arthritis, baldness, cardiovascular diseases (coronary syndrome and angina), diabetes and many others. [2]

The study of peptides cell penetrating mechanisms is a new area of research of great relevance in the effort of designing peptide as drugs. To this respect the prediction and experimental determination of molecular properties related to lipophilicity is crucial. The important role played by lipophilicity and the related descriptors in governing pharmacokinetic [3] and pharmacodynamic events of classical organic drugs has been extensively underlined in recent years. The partition coefficient (P or its logarithm log P) of a solute in two immiscible solvents, in particular octanol/water (P_{oct} or log P_{oct}) is one of the most used lipophilicity descriptor. Thus, methods that can accurately and rapidly yield log P_{oct} of peptides would be a welcome addition to the early screening phase of the discovery process. [4]

For the above mentioned reasons, we decided to apply a widely used tool in drug discovery, VolSurf+ [5,6] to the prediction of the log P_{oct} of small peptides to establish the validity of the approach when it moves away from organic compounds. The role played by peptide dimension in the prediction of lipophilicity was individuated as a main item to be carefully taken into consideration.

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