# Drug Discovery and Design for Complex Diseases through QSAR Computational Methods

* Abstract: - the Quantitative Structure – Activity Relationship models (QSAR) and the complex network theory become important solutions for screening and designing efficient pharmaceuticals by coding the chemical information of the molecules into molecular descriptors.
* Introduction: - any real complex system such drugs, protein, nucleic acids, metabolism, diseases or societies can be numerically characterized and compared according to the relationship properties between its components.
* The graphical methods become an efficient tool to describe complex networks made out of nodes such as atoms linked by chemical bonds (drug), amino acids connected by peptide chemical bonds (protein), nucleic bases linked by a transformation or interaction (metabolism and diseases) or persons connected by a common activity (society).
* The invariant macromolecular descriptors named topological indices (TIs) or connectivity indices (CIs) code the internal information about the structure of a complex system within the Graph or Complex Network (CN) theory.
* The Quantitative Structure Activity Relationship (QSAR) is widely-used for the prediction of drug properties and the Quantitative Protein Disease Relationships (QPDRs) for disease prediction.
* QSAR represents the method to quantitatively correlate the chemical structure with the biological activity or chemical reactivity [*Activity =* f(*physio-chemical properties* and/or *structural properties*)].
* The mathematical models obtained can then be used to predict the biological activity of other chemical structures.
* Graphs and QSAR: - a real network is a collection of objects connected by physical links or common properties. The graph is undirected if there is no distinction between two vertices or directed if there is a difference between two linked nodes.
* In the case of the drug molecules, additional physical and chemical properties of the atoms and molecules are added as weights of the corresponding nodes such as lipophilicity, polarizability, electronic and steric properties.
* First QSAR study was carried out in 1863, when A.F.A. Cros observed that the toxicity of alcohols to mammals increased as the water solubility of the alcohols decreased.
* Louis Hammett added some QSAR studies that correlated electronic properties of organic acids and bases with their equilibrium constants and reactivity.
* A new approach was proposed by Cramer et al. to describe the molecular properties for each field, calculated in a regular grid.
* Vectors have been extracted from these fields by using the principal component analysis and have been correlated with the biological activity. The method was called DYLOMMS (dynamic lattice-oriented molecular modeling system).
* Cramer et al. published a method of comparative molecular field analysis (CoMFA), this molecular field-based method constituted the first real 3D QSAR method and it is more appropriate to describe ligand-receptor interactions, because it takes into consideration the properties of the ligands in their bioactive conformations.
* This method examines the steric fields and the electrostatic fields based on the applied energy function.
* Klebe et al. introduced the comparative molecular similarity indices (CoMSIA), a method of 3D-QSAR analysis, in which, by using a common probe atom, similarity indices are calculated at regularly placed grid points for the pre-aligned molecules.
* One of the modern versions of the QSAR method is the hologram QSAR, a 2D QSAR method that has shown a predictive ability comparable to those of more sophisticated 3D QSAR techniques HQSAR generates specialized molecular holograms that incorporate information about each 2D fragment, and each of its constituent subfragments, implicity encoding 3D structural information that is important for the binding affinity.
* QSAR in Neurology: -