IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Role Of QSAR In Drug Design

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Abstract: Quantitative Structural activity relationship (QSAR) , defined as quantitative correlation of biological activities with physicochemical properties. If we take a series of chemicals and attempt to form a quantitative relationship between the biological effects (i.e the activity)and the chemistry (i.e the structure) of each of the chemicals, then we are able to form a quantitative structure–activity relationship or QSAR. Now a days a newer technique i.e 3D QSAR is also used to overcome the problems of classical QSAR. Some recent version of QSAR such as QSAR-co-x, Dragon 0.7, ALVADESC 2.0, etc. which have some extra features like, QSAR-Co-X provides features for developing linear and nonlinear relationship between models. In this review we have summarized all the data regarding purpose, application, process, and limitations of QSAR.

Index Terms - QSAR, chemistry qualitative, 3D structure, GQSAR, QSARpro biological activities. Predictions.

INTRODUCTION

The identification of new drug required a lot's of synthesis, time and money. For insure the quality, safety, of marketed drug by subjecting drug to various kind of test. due to high risk of drug development failure QSAR required high and time.[1] Healthcare and medicinal system rapidly change over the past years. Rational drug design method reduced the expenses and duration needed in drug designing process in comparison to conventional drug discovery method. QSAR/QSPR studies can be used design and find out to optimize absorption, distribution, metabolism excretion and toxicity profile of identified molecule in various sources.[2] Thus, it can useful to predict the drug discovery failure prior to clinical state in order to reduced drug development cost.

General workflow of developing QSAR :

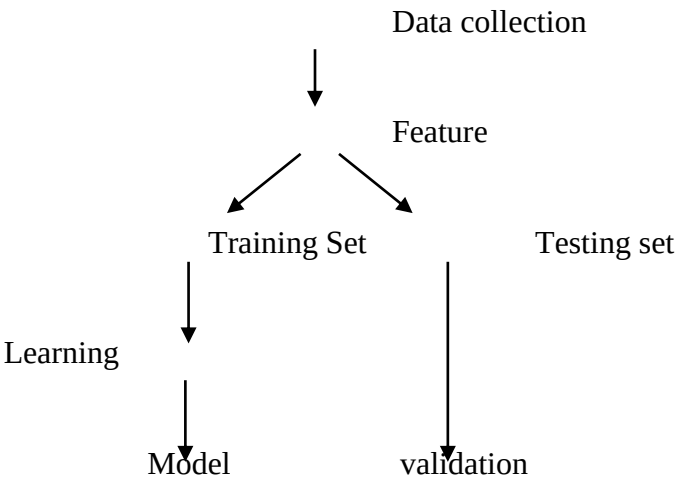

Fig. 1.1

As illustrated in figure 1.1 start taking your data according to property of interest while taking data sheet quality f select quality of data select quality of data important to exclude low quality of data.[2] Following that representation of the collected molecule is done by using features like a molecular descriptor. There are many types descriptors. There are many types of descriptors. There of many types of descriptors out of interest should be removed out of interest should be remove before modeling process. Subsequently the full data set divide into training set and testing set. Prior to learning. The learning process include various modeling methods like multiple linear regression, log regression and machine learning methods are used to develop models, that are describe relation between structure and property of interest.

- **QSAR DEFINATION AND DEVELOPMENT :**

Quantitative structure activity relationship (QSAR) is a computational modeling method describe relationship between the structural properties of chemical compound and biological activities in quantitative manner for a series of compound. QSAR modeling is essential for drug discovery.[3] In QSAR is assumed that the biological activities showed by a related compound is a function of various physical-chemical activity. A major goal of the quantitative structure activity relationship studies to find out mathematical and structural relationship between the physical-chemical property and biological activity.[2]

- **RELATED TERMS :**

Related terms regarding quantitative structured activity relationship like, quantitative structured property relationship(QSPR).Different behavior of chemical properties of molecule have been investigated in the field of QSAR. Some examples of quantitative structured property relation like, Quantitative structured chromatography relationship (QSCR). Quantitative structured toxicity relationship(QSTR). Quantitative structured electrochemistry relationship (QSER). And quantitative structured biodegradable relationship'(QSBR).[3] There are lots of software available for QSAR development and they are either commercial or free. These are important software for drawing chemical structure, interconverting chemical file formats, generating 3D structures, developing QSAR models general purpose of software which have all important features for the QSAR development. The most frequently used software for the structured drawing are chem draw, ACD/ chem sketch and open model software. For the 3D structure generation CORINA, concord, frog, smi23D. Descriptors calculation can be made by using Dragon, software.[2]

PRINCIPLE STEPS OF QSAR INCLUDE-

- Selection of data set and extraction of structural empirical descriptors.
- Variable selection
- Model construction
- Validation evaluation

The first important step in QSAR study is the generation of 3D models. The generation of 3D models. The 3D model needed for the geometric descriptor calculation. The second major step in QSAR/QSPR is the generation of molecular structure description. Selection of most relevant descriptor is third step and it can achieve by using features selection method. The fourth major step QSAR/QSPR study is statistical mapping of toxic end point. The fifth and last step is to validate the model by predicting the activity of compound in the external prediction set.[1]

MOLECULAR DESCRIPTORS :

Molecular descriptors are finding product of mathematical procedure transforming chemical information encoded within molecular structure to a numerical formulae e.g. molecular weight, number and type of atom.

- **0D QSAR:** These are descriptors derived from molecular formula e.g. molecular weight, number and type of atoms etc.
- **1D QSAR:** A substructure list representation of a molecule can be considered as a one-dimensional (1D) molecular representation and consists of a list of molecular fragments (e.g. functional groups, rings, bonds, substituents etc.).
- **2D QSAR-** A molecular graph contains topological or two-dimensional (2D) information. It describes how the atoms are bonded in a molecule, both the type of bonding and the interaction of particular atoms (e.g. total path count, molecular connectivity indices etc.).
- **3D QSAR-** These are calculated starting from a geometrical or 3D representation of a molecule. These descriptors include molecular surface, molecular volume and other geometrical properties. There are different types of 3D descriptors e.g. electronic, steric, shape etc

  .
- **4D QSAR-** Four-dimensional information is described in this type of models, and the fourth dimension is an ensemble of conformation of each ligand.
- **5D-QSAR** Five-dimensional information is described in this type of models, and the fifth dimension is the possibility to represent an ensemble of up to six different induced-fit model[1]

NEW SOFTWARE IN QSAR :

- **ACD/ Chem Sketch-** ACD/ChemSketch is a molecular modelling program used to create and modify images of chemical structures.
- **CORINA-** Is a fast and powerful 3D structure generator for small and medium sized drug molecule.
- **Dragon**-Dragon software provides 5270 software's for calculation.
- **QASR-co-X**- QSAR-Co-X provides features for developing linear and nonlinear relationship between models.
- **CORAL software**- The CORAL is free software to build up quantitative stricture- activity relationship.

- **MSI-Catalyst,Serius**- The parameters used in QSAR is a measure of the potential contribution of its group to a particular property of the parent drug.

- **Tripos-CoMFA**- Comparative molecular field analysis (CoMFA) is a molecular field–based, ligand-based method which helps in building the quantitative relationship of molecular structures and its response property.

APLLICATION'S:

- QSAR quantifying the relation between structure and activity with their physicochemical property basis.

- Possible to make prediction of possible designed compounds before their chemical synthesis of novel analogues.

- It may help to understand the interaction between functional group of designed molecules and their activity of target enzymes or protein.

- Quantitative structure activity relationship (QSAR) has an essential role in drug design process these days, because they are cheaper alternative than the medium throughput in vitro and low throughput in vivo assays.

- In drug discovery and environmental toxicology, QSAR models are now regarded as scientifically credible tool for predicting and classifying the biological activities of untested compounds, drug resistance, toxicity and physicochemical properties prediction.

CONCLUSION :

The methods of quantitative structure-activity relationships which have developed during the past 30 years nowadays are widely applied to describe the relationships between chemical structures of molecules and their biological activities. Many attempts have been made to understand structure-activity relationships in physicochemical terms (or in terms of structural features, using indicator variables for individual substituents and groups) and to design new drugs on a more rational basis . In general, the experimental determinations are very expensive and the QSPR studies allow a reduction of this cost. It is basically used to study the biological activities with various properties associated with the structures, which is helpful to explain how structural features in a drug molecule influence the biological activities. QSPR/QSAR methods can be used to build models that can predict properties or activities. for organic compounds. However, an effective way to encode the structures with calculated molecular structure descriptors are required for accurate models' development. The descriptors incorporated in models' development can provide an opportunity to focus on specific features account for the property or activity of interest in the compounds.

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