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Review Paper

Modern drug design with advancement in QSAR: A review

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Abstract

Over the last 20 years, extensive QSAR studies establish an attractive approach to the elucidation of the modern drug chemistry. In the recent years, constant increase in the performance of hardware and software transformed quantitative structure activity relationship (QSAR) and quantitative structure property relationship (QSPR) into powerful and widely used model for the prediction of many biological properties in the field of medicinal chemistry and bioinformatics. The aim of this article is to give an overview of the modern drug chemistry and the importance of various techniques used in the field of drug chemistry such as bioinformatics, QSAR/QSPR, cheminformatics. QSAR is an effective method in the field of medicinal research into rational drug design and mechanism of drug action. The review attempts to account the scenario of drug design and its related research while using different techniques i.e. QSAR. The paper also deals with the brief account of various methodologies in drug design such as, Artificial neural networks, Multiple linear regression analysis, Partial least squares and Principal component analysis. The paper further extends the different dimensions of QSAR viz. 1D, 2D, and 3D and so on. 3D- descriptors have a strong element of the molecular topology and regarded as essential tool and allow chemist to interpret the results in terms of chemical structure and biological manner. Many applications in computational drug design prediction of structure in the development of drugs purely depend on the 3D structure of the drug molecules. The importance and utility of the 3D QSAR discussed in details. Some of the method, which widely used in QSAR, has been discussed in brief.

Keywords QSAR, drug design, MLR, ANN, 3D QSAR, molecular modeling and computational chemistry.

Introduction

Drug design and discovery

The discovery of drugs and drug molecules has always been the aim of pharmaceutical sciences and, in particular, of medicinal chemistry, which evolved from pharmaceutical chemistry. Half a century ago, pharmacochemistry, the modern expression of pharmaceutical chemistry, as a science whose main interest is the design and development of new pharmacomolecules, was at the beginning of its evolution. Drug design in its broad sense and structure-activity relationship studies are essential and at the heart of medicinal chemistry, and the progress and development of this field of research that has made medicinal chemistry the modern and enormously productive science in recent decades [1]. Drug discovery and development are expensive undertaking. The application of computational technology in drug discovery and development offers considerable potential for reducing the number of hit and trial method in R & D. Today, studies on structure-activity relationships and their influence

on the design of new drugs have rendered them one of the most useful and thus important activities of pharmacochemistry, a modern component science in the group of pharmaceutical sciences [2].

Despite the advances in medical and pharmaceutical sciences, there are still many diseases which are incurable or can only be treated symptomatically, and at a great economic and social cost owing to only moderately effective or even to the lack of appropriate therapeutic agents. Of the 30000 or so diseases or disorders currently known, only one-third can somehow be treated with drugs. Furthermore, there are incurable maladies, like viral diseases (influenza, AIDS), CNS disorders (Alzheimer's disease), cancer and autoimmune disorders, which can be fatal or cause great suffering and disability [3]. Therefore, there is still a great need for more and better drugs—more active and selective, drugs with fewer undesired or toxic side-effects, agents useful in prophylaxis and drugs which will cause as little as possible harmful contamination in the already polluted environment.

The primary objective of medicinal chemistry is the design and discovery of new compounds that are suitable for use as drugs. This process involves a team of workers from a wide range of disciplines such as chemistry, biology, biochemistry, pharmacology, mathematics, medicine and computing, amongst others. The discovery or design of a new drug not only requires a discovery or design process but also the synthesis of the drug, a method of administration, the development of tests and procedures to establish how it operates in the body and a safety assessment. Drug discovery may also require fundamental research into the biological and chemical nature of the diseased state. These and other aspects of drug design and discovery require input from specialists in many other fields and so medicinal chemists need to have outline knowledge of the relevant aspects of these fields.

Drug design explain-
1. Relationship between biological activity and structure.
2. Drug receptor interaction on the basis of various physico-chemical properties.
3. Modify the drug molecule according to the need.
4. The effect of the drug towards the biological responds by various processes.

The historical aspect

4 March 1958 is the golden day o Indian Parliament, when the parliament proposed the government for the development of science. In 1983 Indian government started a principal for the development of science. Since ancient times the peoples of the world have had a wide range of natural products that they use for medicinal purposes. These products, obtained from animal, vegetable and mineral sources, were sometimes very effective. However, many of the products were very toxic and it is interesting to note that the Greeks used the same word pharmakon for both poisons and medicinal products. Information about these ancient remedies was not readily available to users until the invention of the printing press in the fifteenth century. This led to the widespread publication and circulation of Herbals and Pharmacopoeias, which resulted in a rapid increase in the use, and misuse, of herbal and other remedies. Misuse of tartar emetic (antimony potassium tartrate) was the reason for its use being banned by the Paris parliament in 1566, probably the first recorded ban of its type. The usage of such remedies reached its height in the seventeenth century. However, improved communications between practitioners in the eighteenth and nineteenth centuries resulted in the progressive removal of preparations that were either ineffective or too toxic from Herbals and Pharmacopoeias. It also led to a more rational development of new drugs.

The early nineteenth century saw the extraction of pure substances from plant material. These substances were of consistent quality but only a few of the compounds isolated proved to be satisfactory as therapeutic agents. The majority were found to be too toxic although many, such as morphine and cocaine for example, were extensively prescribed by physicians. The search to find less toxic medicines than those based on natural sources resulted in the introduction of synthetic substances as drugs in the late nineteenth century and their widespread use in the twentieth century. This development was based on the structures of known pharmacologically active compounds, now referred to as leads. The approach adopted by most nineteenth century workers was to synthesise structures related to that of the lead and test these compounds for the required activity. These lead-related compounds are now referred to as analogues. Day by day the field of drug design progressively and development of the drugs are now very common practice due advancement in the computer techniques.

The general stages in modern-day drug discovery and design

At the beginning of the nineteenth century drug discovery and design was largely carried out by individuals and was a matter of luck rather than structured investigation. Over the last century, a large increase in our general scientific knowledge means that today drug discovery requires considerable teamwork, the members of the team being specialists in various fields, such as medicine, biochemistry, chemistry, computerised molecular modelling, pharmaceutics, pharmacology, microbiology, toxicology, physiology and pathology. The approach is now more structured but a successful outcome still depends on a certain degree of luck. The modern approach to drug discovery/design depends on the objectives of the project. The (Figure 1) has given below shows the general stages in drug discovery and design.

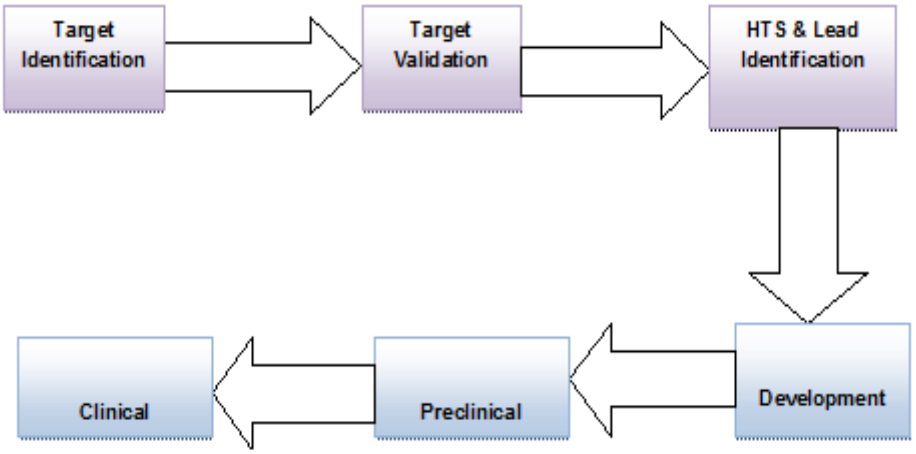

Figure 1: General stages in drug discovery and design

These objectives can range from changing the pharmacokinetics of an existing drug to discovering a completely new compound. Once the objectives of the project have been decided the team will select an appropriate starting point and decide how they wish to proceed. For example, if the objective is to modify the pharmacokinetics of an existing drug the starting point is usually that the drug and design team has to decide what structural modifications need to be investigated in order to achieve the desired modifications. Alternatively, if the objective is to find a new drug for a specific disease the starting point may be knowledge of the biochemistry of the disease and/or the microorganism responsible for that disease. This may require basic research into the biochemistry of the disease causing process before initiating the drug design investigation. The information obtained is used by the team to decide where intervention would be most likely to bring about the desired result. Once the point of intervention has been selected the team has to decide on the structure of a compound, referred to as a lead compound, which could possibly bring about the required change. A number of candidates are usually considered but the expense of producing drugs dictates that the team has to choose only one or two of these compounds to act as the lead compound. The final selection depends on the experience of the research team.

SAR and QSAR

SAR stands for Structure Activity Relationship while the QSAR stands for Quantitative Structure Activity Relationship. SAR deals with the relationship of structure with biological activity while the QSAR accounts the relationship of magnitude of the various structural properties with the biological activity. Compounds with similar structures to a pharmacologically active drug are often themselves biologically active. This activity may be either similar to that of the original compound but different in potency and unwanted side effects or completely different to that exhibited by the original compound. These structurally related activities are commonly referred to as structure–activity relationship (SAR).Perhaps the historically most successful approach to such studies is to use so-called 2D-desceptors, which are based on bonding topology of the molecules. A study of the structure–activity relationships of a lead compound and its analogues may be used to determine the parts of the

structure of the lead compound that are responsible for both its beneficial biological activity, that is, its pharmacophore, and also its unwanted side effects. This information may be used to develop a new drug that has increased activity, a different activity from an existing drug and fewer unwanted side effects. Structure–activity relationships are usually determined by making minor changes to the structure of a lead to produce analogues and assessing the effect these structural changes have on biological activity. The investigation of numerous lead compounds and their analogues has made it possible to make some broad generalizations about the biological effects of specific types of structural change. These changes may be conveniently classified as changing

1. The size, shape and branching of the parent structure
2. Types of substitution and their nature
3. The stereochemistry of the lead compound

The main assumption in the QSPR and QSAR approaches is that the all properties viz. physical, chemical and biological is purely depend on the molecular structure. QSAR is an attempt to remove the element of luck from drug design by establishing a mathematical relationship in the form of an equation between biological activity and measurable physicochemical parameters. These parameters are used to represent properties such as lipophilicity, shape and electron distribution, which are believed to have a major influence on the drug's activity. The structure of the compounds is represented in terms of numerical forms by various descriptors. They are normally defined so that they are in the form of numbers, which are derived from practical data that is thought to be related to the property the parameter represents. This makes it possible to either to measure or to calculate these parameters for a group of compounds and relate their values to the biological activity of these compounds by means of mathematical equations using statistical methods such as regression analysis. These equations may be used by the medicinal chemist to make a more informed choice as to which analogues to prepare. The mathematical structure-property relationships quantify the connection between the structures and the properties of molecules. The relationships are mathematical models that allow the prediction of properties from structural parameters. These features lead us to look for suitable indices for encoding the structural information. We have published a study [3a] on SAR of some benzodiazepines.

For example, it is often possible to use statistical data from other compounds to calculate the theoretical value of a specific parameter for an as yet unsynthesised compound. Substituting this value in the appropriate equation relating activity to that parameter, it is possible to calculate the theoretical activity of this unknown compound. Alternatively, the equation could be used to determine the value 'x' of the parameter 'y' that would give optimum activity. As a result, only analogues that have values of y in the region of x need be synthesized. (Figure 2) given below shows the schematic representation of QSAR equation.

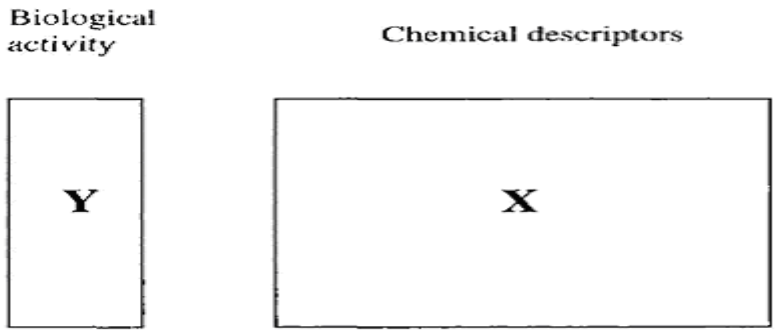

Figure 2: Schimatic representation of QSAR equation

The main properties of a drug that appear to influence its activity are its, lipophilicity, the electronic effects within the molecule and the size and shape of the molecule (steric effects). Lipophilicity is a measure of a drug's solubility in lipid membranes. This is usually an important factor in determining how easily a drug passes through lipid membranes. The electronic effects of the groups within the molecule will affect its electron distribution, which in turn has a direct bearing on how easily and permanently the molecule binds to its target molecule. Drug size and shape will determine whether

the drug molecule is able to get close enough to its target site in order to bind to that site. The parameters commonly used to represent these properties are partition coefficients for lipohilicity, Hammett's constants for electronic effects and Taft's steric constants for steric effects.

The information obtained is composed of mathematical equations relating the chemical structure of the compounds to a wide variety of their physical, chemical, and biological properties. Once a correlation between structure and activity/property is found, any number of compounds, including those not synthesised yet, can readily be synthesised with desired properties. Hence, it is possible to select the most promising compounds for synthesis and testing in the laboratory. Quantitative structure–activity relationship (QSAR) describes how a given biological activity can vary as a function of molecular descriptors derived from the chemical structure of a set of molecules. Thus, a model containing those calculated descriptors can be used to predict responses of new compounds [3, 4].

Quantitative structure-activity relationship (QSAR) and quantitative structure-property relationship (QSPR) studies are undoubtedly of great importance in modern chemistry and biochemistry. To obtain a significant correlation, it is essential that appropriate descriptors be used, regardless of whether they are theoretical, empirical or derived from readily available experimental characteristics of structures. Many descriptors reflect simple molecular properties and can thus provide insight into the physicochemical nature of the activity/property under consideration [5-7]. Quantitative structure activity and structure property relationships (QSAR/QSPR) are of great importance in medicinal chemistry and biochemistry, because they can accelerate the development of new compounds for use as drugs, materials or additives by computer screening of molecular structures that can predict the desired properties prior to laboratory tests.

Activities used in QSAR include chemical measurements and biological assays. For example, biological activity can be expressed quantitatively as in the concentration of a substance required to give a certain biological response. Additionally, when physicochemical properties of structures are expressed by numbers, one can find a quantitative structure-activity relationship between properties and structures. The mathematical expression can then be used to predict the biological response of other chemical structures. QSAR are currently being applied in many disciplines, such as drug design and environmental risk assessment. Using QSAR, an estimate of the activity of a chemical from its molecular structure can be obtained; QSAR offers the possibility for screening a large number of chemicals in a short time and at low cost [8-10].

The basic idea behind the QSAR/QSPR is to find the appropriate function i.e. physio-chemical, topological and other properties by using the information which given in the structure of the molecule. In fact QSAR, as a technique attempting to summarize chemical and biological information in order to generate relationships between structure and biological activity, hastens the drug design and aims to develop these compounds.

$$\text{Property} = F(\text{Structure})$$

So, we can say that the biological properties of any molecule are the function of the structure i.e. any change in structure will definitely affect the biological activity.

Classification of QSAR methodologies

Based on dimensionality

Most often the QSAR methods are categorized into following classes, based on the structural representation or the way by which the descriptor values are derived:
1D-QSAR Correlation of fundamental molecular properties viz. pKa, log P with biological activity.
2D-QSAR Correlation of various 2D properties i.e. physio-chemical properties with biological activity.
3D-QSAR Correlation of various 3D properties which surrounding the molecule.
4D-QSAR Introducing the ligand receptor interaction of the drug molecule with the 3D properties.
5D-QSAR explicitly representing different induced-fit models in 4D-QSAR
6D-QSAR further incorporating different salvation models in 5D-QSAR.

This paper emphasizes the role of 3D- QSAR in the field of drug design, so we have discussed the details of 3D-QSAR later on this paper.

Based on the methods used in QSAR

Sometimes QSAR methods are also classified into following two categories, depending upon the type of correlation technique employed to establish a relationship between structural properties and biological activity: multiple linear regression (MLR), partial least-squares (PLS), and principal component analysis/regression (PCA/ PCR). Non-linear methods consisting of artificial neural networks (ANN). All the methods briefly explain below-

MLR (Multiple Linear Regressions)

The multiple linear regression method is used to screen the appropriate descriptor from a large pool of descriptor. Multiple linear regressions (MLR) is a method used to model the relationship between two or more explanatory variables and a response variable by fitting a linear equation to the observed was employed to correlate the binding affinity and molecular descriptors. The (Figure 3) has given below shows the graphical representation of the observed and calculated activity for any data set using multiple linear regression analysis. We have published a research paper on TIBO derivatives by using MLR [10a].

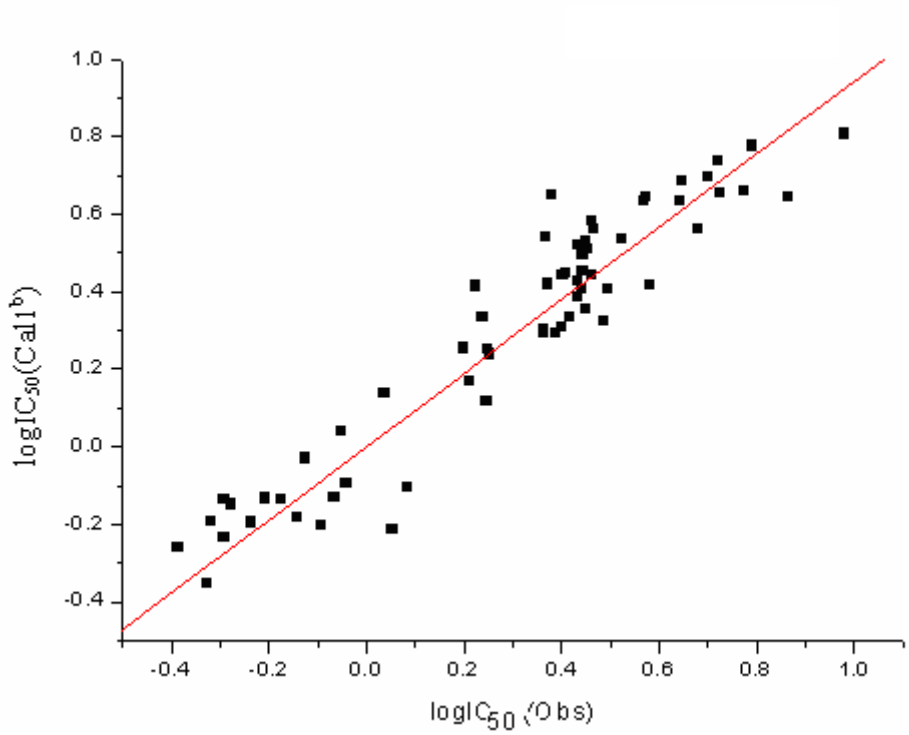

Figure 3: Graphical representation of MLR between observed and calculated activity

PLS (Partial Least-Squares)

PLS is a method for constructing predictive models when the factors are many and high collinear. It is used in many applied sciences. PLS is often referred as the classical algorithm (Figure 4). The algorithm choice depends on the shape of data matrices. The updating procedure is one of the computational ways to solve the new algorithms by using small updating matrices or by orthogonalization procedure. The classical PLS algorithm is always a problem for the computational chemist however this difficulty can be overcome by using only one variable in modeling. In PLS components are selected that give "maximal" reduction in the covariance X^TY of the data. Hence, e Partial Least Square method will give the minimum number of variables, which is essential to generate the model and at the same time to gather the information about the molecule. PLS has been applied to monitoring and controlling industrial processes; a large process can easily have hundreds of controllable variables and dozens of outputs. However, when we need to predict and if there is no practical limit to the number of measurable factors then PLS can be a useful tool. It also a popular method for soft modelling in industrial applications.

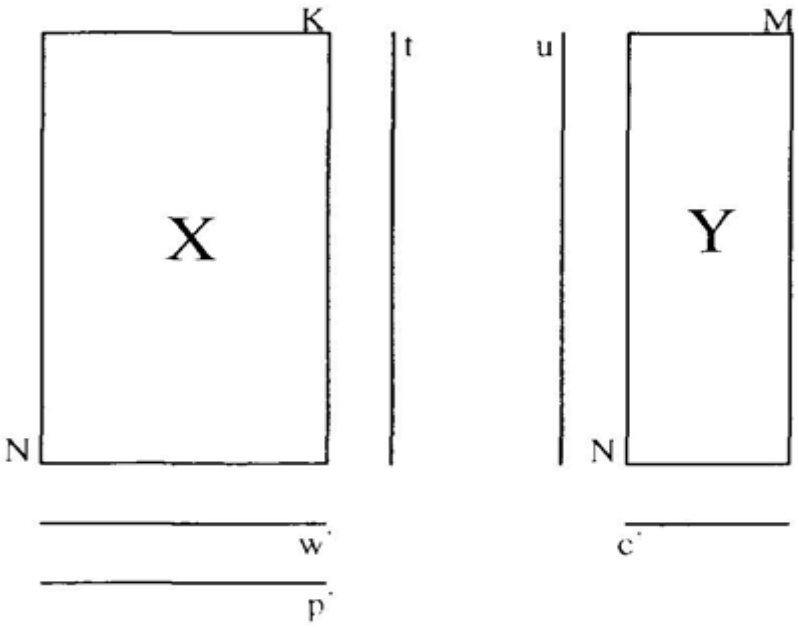

Figure 4: Graphical representation of classical PLS algorithm

ANN (Artificial Neural Network)

In recent years, artificial neural networks have been used widely. Neural networks (ANN) can be used to generate predictive models of quantitative structure–activity relationships (QSAR) between a set of molecular descriptors obtained from the MLR and observed activity. It is generalization of mathematical models of biological system. The important factor about the ANN is the ability to build model of the problem using data from experimental measurements of the problem domain. With the advancement in the field of drug design ANN have been applied to solve the problem of various pharmaceutical process and product development. The (Figure 5) given below shows the schematic representation of ANN. Neural networks are model-free mapping devices that are capable of capturing complex nonlinear relationships in the underlying data that are often missed by conventional QSAR approaches. However, neural networks are known to be unstable, in the sense that minor changes in the training data and/or training parameters can have serious consequences in the generalization ability of the resulting models.

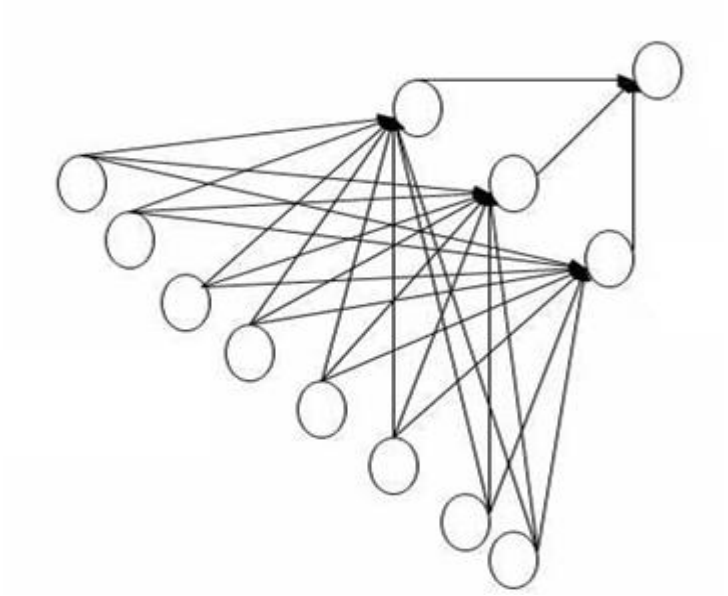

Figure 5: Schematic representation of ANN

Purpose of QSAR

Primary focus of any QSAR is to develop the best drug model to overcome the difficulty of the trial and error methods. This is the only way to reduce the cost and time of the synthesis of the drug, so as to improve the biological activity of the drug molecule. From these relationships we can develop models, and the validity and predictiivty of the model can also tested with various statistical tools. There are many practical purposes of a QSAR and these techniques are utilized widely in many situations. Some of them given below-

1. To reduce the trial and error synthesis drugs, which also reduce the time and cost of the synthesis of the drug in the laboratory.
2. To enhancing the importance and role of greener chemistry specially for environmental purposes with the elimination of waste and less toxic compounds.
3. To save time and effort in clinical trial specially the animal trial and preclinical trial.
4. With the help of advanced mechanism of the drug with the specific enzymes and proteins, the idea to synthesis the more potent drug for the diseases.
5. To comprehend and rationalize the mechanisms of action within a series of chemicals.

Applications of QSAR

With the advancement in the field of drug design and medicinal chemistry the applications of QSAR spread on the various filed of drug discovery. Few of them is given below-
1. To rationalization of new leads compound with enhance biological activity.
2. To identify the toxic chemicals and toxicity of the drug molecule before the synthesis. This will reduce the toxicity for environmental species and other biological system.
3. The optimization of pharmacological and pesticidal activity.
4. The identification and selection of the compound in order to get the best biological responds with better and optimal pharmacokinetics properties.
5. The rational design of numerous other products such as surface-active agents, perfumes, dyes, and fine chemicals.
6. To identify the role of various properties to design the drug molecule and to know the better properties to improve the biological activity.

Limitations of classical QSAR

Although the classical QSAR methods are much simpler and faster than 3D-QSAR approaches. They include clearly-defined physio-chemical descriptors and are best suited for the analysis of large number of compounds and computational screening of molecular databases. But still the day by day challenges in the field of drug design shows that this one also has some limitations. Few of them given below-

1. The biomolecules mainly are in complicated three dimensional structure while the classical QSAR only deals with the 2D-structures.
2. While using 2D descriptor only limited number of descriptor taken into account, which has the limitation of the traditional method.
3. No representation of stereochemistry or 3D-structure of molecules, regardless of their availability.
4. No predictivity of generated model, so it is difficult of go for the synthesis on behalf of the 2D model.
5. 2D QSAR models of better by the chance correlation rather than the actual prediction.
6. Requires considerable knowledge of substituent constants in physical organic chemistry to design a molecule, since classical QSAR equation do not directly suggest new compounds to synthesize

3D- QSAR

Three-dimensional quantitative structure–activity relationship (3D-QSAR) techniques are the most prominent computational means to support chemistry within drug design projects where no three-dimensional structure of the macromolecular target is available. The primary aim of these techniques is to establish a correlation of biological activities of a series of structurally and biologically characterized compounds with the spatial fingerprints of numerous field properties of each molecule, such as steric demand, lipophilicity, and electrostatic interactions.

Any 3D QSAR method wouldn't be tried for a dataset unless the experiment expects that the study wil provide useful 3D structure insight the drug molecule. Even before computers, medicinal chemists knew that a set of molecules will typically display an understandable structure–activity relationship [11].

Usually this is manifest in the observation that the smaller the change in the structure of the molecule, the less likely is there to be a change in its biological properties. The similarity principle is another way to say the same thing: compounds with similar chemical and physical properties also have similar biological properties [12]. In QSAR the similarity principle is considered to apply within a series or structural class only [13], although the pharmacophore hypothesis generalizes the similarity to 3D properties independent of the underlying structure diagrams of the compounds [14-15]. Another important observation is that the effect on biological activity of changing a substituent at one position of a molecule is often independent of the effect of changing a substituent at a second position, quantified in the early Free–Wilson QSAR method [16]. Supplanting these qualitative insights by 3D quantitative structure–activity relationships was accomplished by the conscious or unconscious incorporation of insights from many different disciplines.

Structural chemistry provides valuable insights into why changing a substituent on a molecule might change its biological activity. For decades scientists have realized that the three-dimensional arrangement of dispersion, electrostatic and hydrophobic interactions, as well as hydrogen-bonds, determines the strength of intermolecular interactions [17]. Small-molecule crystallography has contributed greatly to our knowledge of the structural aspects of intermolecular interactions [18-21].

Quantum chemistry changes focus from the nuclei of the atoms, the traditional structure, to the electrons of molecule. Today's computers have changed this discipline from one practiced by only devoted experts [24] to one that laboratory chemists can practice or at least set up on their desk-top computer. Although *ab initio* methods remain the benchmark method, semiempirical quantum mechanical methods allow one to calculate fairly accurately the molecular structure and electronic properties of almost any organic molecule — one doesn't need numerous parameters to do so [22-25]. Recently developed solvation models [26-29] expand the scope of problems that one can tackle. Although physical organic chemistry traditionally focuses on the rate and equilibrium constants of organic reactions [30], it has provided both a precedent and an understanding that has been critical to the development of 3D methods. First, it has provided methods for the quantisation of the electronic, steric and hydrophobic effects of substituents on the reaction centre. Second, it demonstrated that multivariate statistical analysis can suggest the physical basis of biological structure-activity relationships, QSAR [31–33]. It provided the jump-start to combine molecular modelling and statics into 3D QSAR.

Reasons for choosing 3D- QSAR

3D QSAR method describes the properties of the molecules by their calculated interaction energies with the binding site. The era of quantitative analysis for the correlation of molecular structures with biological activities started in the 1960s from the classical equation for 2D-QSAR analysis proposed by Hansch [34]. Since then a variety of QSAR approaches have been reported [35-39]. The first applicable 3D-QSAR method was proposed by Cramer et al. in 1988 [40]. His program, CoMFA, was a major breakthrough in the field of 3D-QSAR. The primary aim of 3D-QSAR methods is to establish a correlation of biological activities of a series of structurally and biologically characterized compounds with the spatial fingerprints of numerous field properties of each molecule, such as steric demand, lipophilicity, and electrostatic interactions. Typically, a 3D-QSAR analysis allows the identification of the pharmacophoric arrangement of molecular features in space and provides guidelines for the design of next-generation compounds with enhanced bioactivity or selectivity. No 3D-QSAR method would be applied to a data set unless one expects that the analysis will reveal insights into useful 3D structure–activity relationships. There is no perfect way to find the accuracy of potency forecast, because each method has different distribution of potency in the test set. Since chemists and biologists know that 3D properties of molecules govern biological activity, it is especially informative to see a 3D picture of how structural changes influence biological activities. Approaches that do not provide such a graphical representation are often less attractive to the scientific community. An advantage of 3D-QSAR over the traditional 2D-QSAR method is that it takes into account the 3D structures of ligands and additionally is applicable to sets of structurally diverse compounds, though the other direction can also taken into consideration but still the need to go through the deep work in 3D aspects because it provides the most fundamental knowledge about the biomolecules behaviour.

Progress in 3D-QSAR approaches

With the development in the computer techniques and internet resources the progress of 3D- QSAR attracts the attention of the medicinal chemists. 3D-QSAR is a broad term encompassing all those QSAR methods which correlate macroscopic target properties with computed atom-based descriptors derived from the spatial (three-dimensional) representation of the molecular structures [41-44]. QSAR is a broadly used tool for developing relationships between the effects (e.g. activities and properties of interest) of a series of molecules with their structural properties. It is used in many areas of science. It is a dynamic area that integrates new technologies at a staggering rate. There have been many recent advances in the applications and methodologies of QSAR. In fact, 3D QSAR model simply provides a summary of how changes in the structure of ligand affect its affinity for a target molecule. So, finally summarizing the above, we can say that the importance of QSAR in drug designing is very essential and to overcome the problem of hit and trial, it should be used at large scale.

Conclusion

QSAR 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. The various evidences have proven that the 3D QSAR techniques will continue to make a valuable contribution to the analysis of structure activity relationship. The emerging field of 3D QSAR help to reduce the problem of traditional 2D QSAR. Because of the accuracy and very fast speed the 3D QSAR model help to design the ligand- macromolecule complex. So, it can be expected that the 3D QSAR will continue to impact the analysis of high throughput screening structure-activity data. The field of cheminformatics is newly introduced and gain the importance for the researcher in development of new drugs. Different software packages play vital role in this direction. QSPR studies are an important tool for research and knowledge of chemical compounds and it has been frequently used in medicinal chemistry and molecular design to investigate new drugs. It is especially useful when the experimental determination of properties is very complex, the handling of materials may involve some risk, or determinations may not be easy in cases where compounds can quickly degrade. In general, the experimental determinations are very expensive and the QSPR studies allow a reduction of this cost. Thus, the QSPR/QSAR approach conserves resources and accelerates the process of development of new molecules. The importance of 3D-QSAR in the new era of drug design and computational chemistry cannot be ignoring. It provides the wide platform for the researcher and scientist to work towards in this direction, though more dimensions viz. 4D-, 5D- and 6D- also attract the researcher but the main origin is the 3D-QSAR because it gives the fundamental aspects of every part of the drug molecule.

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