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Drug Design and Development Based on Virtual Screening and High Throughput Screening: A Combination of *In Silico* Prediction and Experimental Research

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The global need today is a healthy lifestyle superseding the threats of the polluted environment. In this regard, healthy lifestyle and food habits considerably shape our health. However, drugs also play a crucial role in alleviating us off the signs and symptoms of diseases. Drugs that are target specific in addition to having high therapeutic index and low toxicity profile exhibit much significance in the field of drug discovery and experimental research. Thus with this aim of searching for drugs with high activity and low toxicity, a great deal of recent research has been oriented towards design and development of new chemical entities that would lead to the identification of the most active moiety targeted against specific biological response [1]. The pathway involved in the design of a new drug moiety comprises of a combination of several novel theories in the field of drug development and discovery. The aim is to reach the target along a simple pathway with is both cost effective and time saving which would prevent wastage of valuable research.

The process of design and development of drugs is a tedious one and requires the involvement of both *in silico* and experimental methodology. Experimental research involving synthesis of drug molecules followed by *in vitro* and *in vivo* studies is the ultimate concept in the process of new drug discovery. However, the process of searching for new drug moieties involving experimental methodology only involves the prime drawback in being the 'black box method'. The synthesis of new chemical entities targeting a specific response is based on changing substitution pattern of existing active molecules. However, no prior knowledge is available regarding the effect of new substitution on the activity profile of the molecules resulting in synthesis of huge number of false hits. Thus the synthesis process alone behaves as a trial and error method making the discovery of new drug fulfilling the desired objective more and more difficult. Over the past decades, the drug discovery pathway has been traversed extensively by *in silico* methodology. The concept of computer aided drug design (CADD) has eased the pathway leading to discovery of new drug molecules [2]. The CADD methodology involves design of new chemical entities based on a precise knowledge about their biological pharmacophore. Moreover, the designed compounds are sorted and subjected to experimental research based on their predicted activity data and patter of interaction with the target receptor as reported from the quantitative structure-activity relationships (QSAR) analysis and docking studies. On the contrary, it is also not possible to identify the activity of new chemicals with the application of only CADD methodology without involving *in vitro* and *in vivo* analysis of the designed compound. Thus combining both the concepts of CADD and experimental research helps to efficiently achieve the desired goal of mining for new drugs.

Thus the modern concept for drug discovery based on *in silico* prediction followed by synthesis and experimental analysis of selected compounds involves the concept of 'virtual screening' [3] and 'high throughput screening' [4]: a widely accepted protocol for searching of database libraries and synthesising active chemical entities. The process involves searching of database libraries targeting a specific response. Molecules selected for a specific response are subsequently filtered for their drug likeliness based on Lipinski's filter and those fulfilling the ADMET (absorption, distribution, metabolism, excretion and toxicity) parameters are considered for further analysis. The filtered molecules are again sorted based on their biological pharmacophore and the selected ones are analysed for their ability to in-

teract with target receptor. The final set of molecules is subjected to activity prediction and he molecules with higher range of activity profile constitute the lead compounds that determine the process of synthesis and analysis leading to discovery of hit molecules. A critical step in the process of drug discovery is the identification of a proper lead compound or a given molecular target [5]. Traditionally high-throughput screening (HTS) of large chemical libraries served as a source for identification of novel lead compounds. Moreover, advances in high-throughput (HT) strategies for structure determination have yielded a large number of three-dimensional structures for several therapeutically relevant targets. These structures constitute the basis of synthesis and analysis of their activity potential. Subsequently, hit molecules are identified based on the results of *in vivo* analyses of the activity of the molecules together with their toxicity profile.

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