

PREFACE

***Sarve bhavantu sukhinah sarve santu nira mayah
Sarve bhadrani pashyanttu maa kaschit duhkh bhaag bhavet.***

This is the saying of our religious books. It is the heart of our Indian culture but now in present era we have forgotten these values. We, the humans are children of nature but now we are trying to become its master and exploit the natural products. The exploitation of natural resources leads to disturbance in natural equilibrium and as a result the natural balance gets damaged. The nature fulfills the loss in form of fatal diseases. Thus as a result new diseases are emerging day by day. Our changing life style is also responsible for certain diseases.

The challenge is how to get rid of the diseases with which humanity is suffering .Man is in search of remedy to get rid of any sort of ailment from the times immemorial. The diseases like Hepatitis, Aids, and Cancer that are considered uncontrolled and incurable are under investigation and efforts are going on to search a very potent, less toxic drug. The interest in cancer has remained strong over the years and so have been the case for anticancer agents. It is one of the most formidable diseases of the world. In fact, if there is any disease, which the mankind is still most afraid of, it is cancer. Cancer is not one disease, but a group of diseases affecting different organs and systems of the body. It develops due to the abnormal and uncontrolled cell division, frequently at a rate greater than that of the most normal body cells. Although cancer mortality is second to heart diseases, the first is steadily increasing, while the latter is levelling off. The agony of cancer patients and the financial burden to families add to

the dread of cancer. Although it is commonly said that prevention is better than cure, efforts to provide preventive measures to cancer have not been very effective, as variety of chemicals and environmental factors can cause cancer. **Thus** once the cancer has developed, one has to resort to its treatment. There are four major modalities for the treatment of the cancer: **(1)** surgery, **(2)** radiation therapy, **(3)** immunotherapy, and **(4)** chemotherapy. Surgery cannot be applied when the disease has spread throughout the body, and radiation therapy damages not only the cancerous cells but also the normal cells. **Thus** in this situation, the only treatment for the disseminated cancer is chemotherapy, although immunotherapy -manipulation of immune response-holds encouraging promise, but it is still in its infancy. Chemotherapy is today providing increasing cure rates in many forms of human cancer. Because of our day by day progress in understanding the effects of drugs on cells, both normal and cancerous; there has been a continued improvement in this mode of cancer treatment.

The ease and success of finding the better drugs for any disease depends upon how best we can rationalize the design of the drugs. The rational design of an agent with specific activity towards a selected target requires that this target be so pre-cisely defined that it can be hit selectively in the presence of other identical or similar targets. With regard to cancer, there is little information on unique characteristics of cancer cells that may be exploited in the investigation of new agents. Nonetheless, the useful anticancer drugs are being produced but mostly based on empiricism. The mechanism by which the anticancer drugs selectively kill cancer cells has not been clearly established, but evidence points out that these drugs might interfere with the synthesis or function of nucleic acids or with the mitotic process itself

In spite of the presence of large number of drugs for their treatment, the side effects associated with them has always inspired new research in these areas. Drug design is of cardinal importance in the drug discovery process. The two steps of lead generation and lead optimization leading to the identification of target molecule for drug development (discovery phase) usually take 5-6 years followed by 7-8 years time required for detailed toxicity and clinical studies (development phase). In drug discovery phase, the designing of biologically active molecules on a rational basis is of major concern to a medicinal chemist.

During the present studies Quantitative Structure Activity Relationship [QSAR] technique is being applied on some anticancer drug series. QSAR for drug receptor interaction are a subset of structural property correlation in which a variety of chemical and physical molecular properties is employed to define the association between structure and property. Such QSARs are wide spread in medicinal chemistry since the advent of cheap and high speed computing technologies in the past 20 years. They rely on the ability to examine multiple relationships between physical properties and biological activities. The correlation equation between biological activities and physico-chemical parameters of the series of drug is established and in this way the effect of structural parameters of drug on their biological activities is being highlighted during interaction with receptor site. Best-fit equation will be developed and predictions will be made.

The approach is clearly useful in probing, albeit indirectly, the nature of the interaction forces between drug receptor as well as for predicting active compounds ahead of simple cumulative synthesis. . The advances in quantitative structure-activity relationship (QSAR) studies have widened the scope of rationalizing the drug design

and finding the mechanisms of drug actions. It is, therefore, expected that a critical review of QSAR studies on anticancer drugs would be of immense help in providing a greater prospective to the rationalization of designing better agents and to the understanding of their modes of action. *QSARs* have proven their worth in the interpretation of mechanisms of inhibition of a number of enzyme systems and in elucidating the modes of actions of local anaesthetics and a variety of drugs acting at the central nervous system.

Thus correlating the physico chemical properties of compounds to their biological activity is a powerful tool in designing new potent drug, having higher therapeutic index and lesser toxic effects. This correlation study will hopefully minimize the number of compounds that synthetic chemist should prepare, also save time and expenses needed in synthesis work as well as their testing, to discover new drug.