



## AN OVERVIWE: DRUG DISCOVERY AND CHEMISTRY OF HETEROCYCLIC COMPOUND

**Pravin Sanjay Sake<sup>\*1</sup>, Dr. Manoj S. Charade<sup>2</sup> and Varsha Vasant Kamble<sup>3</sup>**

<sup>1</sup>Department of Pharmaceutical Chemistry, Shivaji University of Kolhapur, Government College of Pharmacy, Karad.

<sup>2</sup>Assistant Professor & Head PG Department, Government College of Pharmacy, Karad.

<sup>3</sup>Department of Quality Assurance, SNTD University, C.U. Shah College of Pharmacy, Juhu, Mumbai.

**\*Corresponding Author: Pravin Sanjay Sake**

Department of Pharmaceutical Chemistry, Shivaji University of Kolhapur, Government College of Pharmacy, Karad.

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### ABSTRACT

The process of drug discovery can be described as the identification and validation of a target disease and target interact with that chemical compound in discovery and development. This interaction may be inhibit, foster or otherwise change the activity of the target. Development of drug involves fulfilled all requirements that have to be met before a new compound can be consider as ready for testing in the first time for human subjects. Testing of drug is done by preclinical and clinical trials.<sup>[1]</sup> The pharmaceutical industry on research-based has increasingly due use of modern medicinal chemistry methods, such as molecular modelling, the structure-activity relationships (SAR) can study by these powerful tool. These methodologies also used to study the pharmacodynamics data (e.g., selectivity, affinity, efficacy, potency) as well as pharmacokinetic properties (ADMET: absorption, distribution, metabolism, excretion and toxicity). The field has progressed due to advances in bio molecular spectroscopic methods such as X-ray crystallography and nuclear magnetic resonance (NMR), which have enabled striking progress in molecular and structural biology. These spectroscopic methods which have allowed to more than 100,000 the resolve three-dimensional molecular protein target structures that means providing crucial structural information about drug targets of macromolecule. Both academia and industry SBDD and LBDD approaches have been applied as valuable drug discovery tools. These approaches has been successfully employed in a number of investigations due to structural, chemical and biological data.<sup>[1,2]</sup> Heterocyclic chemistry is one of the branch of chemistry dealing with synthesis, properties, and applications of heterocyclic compound. Heterocyclic chemistry began in the 1800s, in 1818 something developing: in 1832 isolation of alloxan from uric acid by Brugnatelli, obtaining the furan by reaction with sulphuric acid in 1832<sub>s</sub>, dry distillation used for obtaining of Pyrrolin 1834.

**KEYWORDS:** Drug Discovery, Heterocyclic Chemistry etc.

### INTRODUCTION

The process of drug discovery can be described as the identification and validation of a target disease and target interact with that chemical compound in discovery and development. This interaction may be inhibit, foster or otherwise change the activity of the target.

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### MATERIALS AND METHODS

**Drug discovery can be divided roughly into two categories**

#### a. Ligand Based Drug design (LBDD)

In LBDD, utilized knowledge of ligands to develop pharmacophore model or element which containing all structural features for bind to a target active site (protein, receptor and enzyme) because three-dimensional molecular protein target structure is not known. i.e. enzyme structure not possible determined by X-ray crystallography and NMR spectroscopy.<sup>[4,5]</sup>

#### b. Structure-Based Drug Design (SBDD)

In SBDD, structure of target protein is known and all tested compounds for interaction and bio affinity can be calculate by the process of docking; those shows highest interaction with target protein... to helpful for design a

new drug molecule, SBDD proceed through multiple step before the optimized lead reached into clinical trials. The first step isolation, purification and determination three-dimensional molecular structure of the target protein through three main methods: like X-ray crystallography, homology modeling or NMR spectroscopy, next step is lead identification and then lead optimization. Useful compounds comes through virtual screening of different databases are placed into drug target active site of a selected region (protein, enzyme, receptor).

Lead compound selected based on those compound have highest of steric, hydrophobic, electrostatic interaction with the active site of target protein as function of ranking and scoring. Once lead compound has been identify next aim is lead optimization in which improve potency, selectivity and reduce toxic effect by modification chemical structure.<sup>[4,6]</sup> Top ranked compound used evaluations of biological properties, such as potency, affinity and efficacy, are carried out using diverse experimental platforms. SBDD is most important tool for discovering lead compound.<sup>[6]</sup>

### Heterocyclic chemistry

“Hetero” means “different” it’s derived from the Greek Word. Heterocyclic compound is cyclic organic compounds which containing more than one hetero atom in cyclic ring system (oxygen, nitrogen, sulphur.....) where heterocyclic compound are during literature survey is observed that more than 85-90% latest marketed drug which has been discovered containing heterocyclic because it has important in the chemistry and biological system. Heterocyclic compound specific physiochemical property that significant role in metabolism in living cell and treating various disease. Many heterocyclic compound are five and six membered which containing most of hetero atom is oxygen, nitrogen and sulphur in ring system. e.g. Pyridine, purine, thiouracil.

Amino acid of drug containing the heterocyclic compound are proline, histidine, and pyridine example of drug is vitamin such as thiamine, riboflavin, pyridoxine, folic acid etc. The heterocycles extensively used due to its important in photochemistry, biocidal formulation agriculture, electronics, biology, optics, polymer science, additive and modifier as industrial application.

We know that most of near about all drug contain heterocycles, such as antitumor, antibiotic, anti-inflammatory, antidepressant, antimalarial, anti-HIV, antimicrobial, antibacterial, antifungal, antiviral, antidiabetic activity and various natural products are and also applicable for developing sanitizer, corrosion inhibitor and copolymers.<sup>[7,8,9]</sup>

#### a) Nomenclature of heterocyclic chemistry

Name for Heterocyclic compound is given by using appropriate suffix depending upon ring system and

number of heteroatom as well as type of heteroatom or element such as oxygen, nitrogen, sulphur and other hetero atom. Some following example use suffix for element.

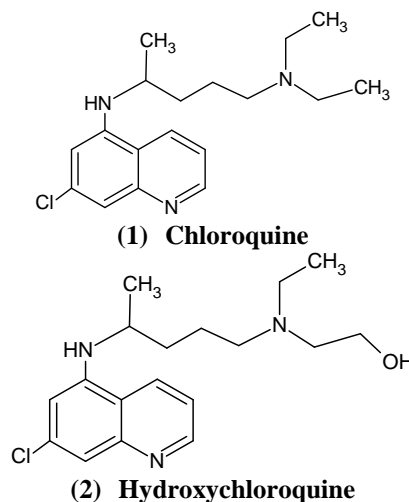
**Table 1: Nomenclatures of heterocyclic compound.**

Sr. No	Element	Valences	Prefix
1	Oxygen	II	Oxa
2	Selenium	II	Salena
3	Sulphur	II	Thia
4	Nitrogen	III	Aza
5	Phosphorus	III	Phospha

#### b) Application of Heterocycles in Drug Discovery:

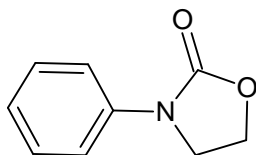
Most of Common Fragment was used in drug discovery as heterocyclic ring by modification and optimizing to until to lead molecule. Following some Application was in drug design

(i) Antimalarial Activity: Malaria is Protozoan parasite disease which is caused by Plasmodium falciparum, Plasmodium vivax, plasmodium malriae and Plasmodium Ovale etc. 4 amino Quinoline used for discovering of Antimalarial drug such as Chloroquine(1), Hydroxy Chloroquine (2), 8 Aminoquinoline etc.<sup>[10]</sup>



(ii) Anti-inflammatory Activity: These are non-Steroidal drug which contain heterocyclic ring for treatment of pain, Fever and redness due to inflammation to body response to tissue injury this is triggered by releasing of various chemical mediators such as Prostaglandins, Histamine, Serotonin and Kenin like peptide substance.

(iii) Antibacterial activity: Bacteria is unicellular organism which may classified as gram positive and gram negative, they further differentiate by staining. E coli is Cause to urinary tract infection to treat UTI infection by Heterocycle ring such as 3 aryl 2 Oxazolidindione (3) which act as antibacterial Drug. This drug decrease bacterial infection by inhibition of bacterial protein synthesis.



(3) 3 aryl 2 Oxazolidindione

(iv) Heterocycles Application in Agriculture: Heterocyclic ring key potential role development of new pesticides, herbicides, insecticides, rodenticides and fungicides etc. These also used in formation of novel plant growth stimulator and regulators. Nicotine is disturb the central nervous of insect which is widely used as insect repellent.<sup>[10]</sup>

(v) Most biological active heterocycle is aromatic form which is diversified application in development new potential active compound in drug discovery. Heterocycles are found in carbohydrate, amino acid, protein, vitamin, resins, alkaloids and aromatic heterocycles contain O, N and S is hetero atom that's why they medicinally important, possess desire biological activity such as anti-inflammatory, analgesic, antibacterial, Antifungal, Antiviral, Anticancer etc.<sup>[10]</sup>

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