

# NATURAL LEAD COMPOUND IN DRUG DESIGN

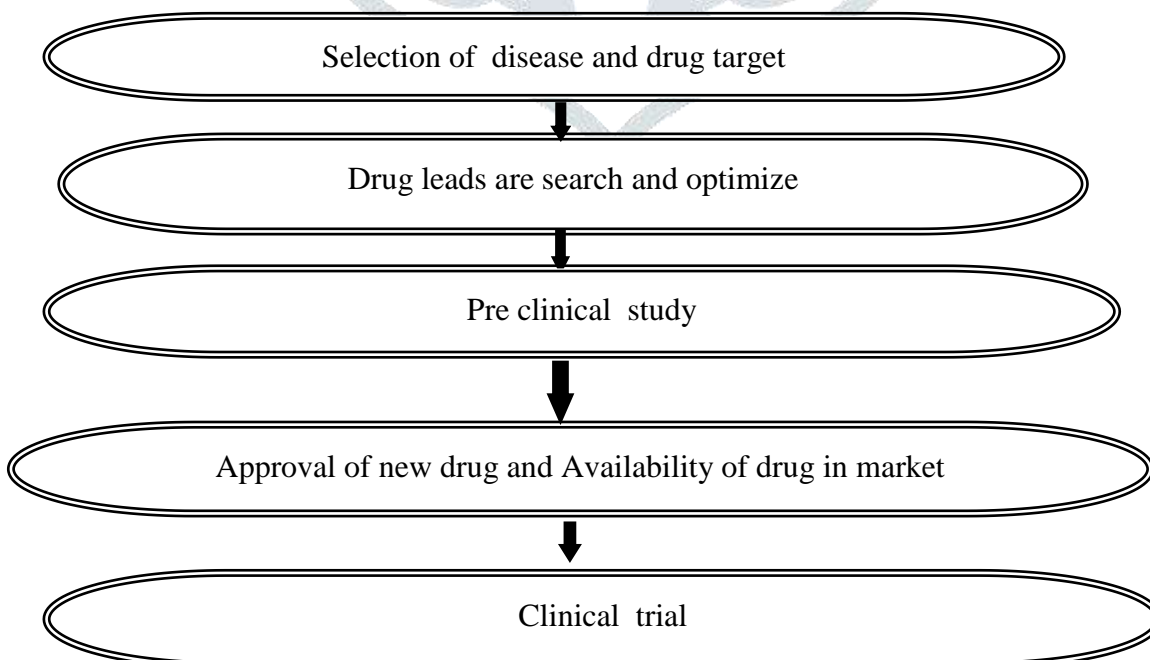
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## Abstract:-

Traditionally, it is highly time consuming and expensive process to design ,development and launching of new drug. Natural process research is increasingly Being combined with computer aided drug design technique by the application of chemo informatics method ,we analyze (quantify ) chemical diversity and structural complexity and distribution in chemical space. During this period of new drug development involves around 10-15 yrs and invest high cost,This is done by various researchers and scientist from various field and discipline .The discovery of new drug from natural product are new strategic option in the field of new drug discovery and used as a lead for the further process. During the last decades a large number of biological active compound was screened out from the natural product as a new drug lead compound .The natural product as a new drug lead compound .the natural sources include Plant ,Animal ,Marine-organism ,mineral and micro –organism etc..

## Introduction :-

The discovery and development of new chemical moiety with some biological activity ,which are works on increasing the therapeutic properties of chemical used in the various ailments in human and animals ,traditionally ,in the development and launching of new drug development and launching of new drug is a much more time taking and expensive process involves following stages;



Natural drug product is a biological active compound that are obtained by the living (Plant, Animal, Micro-organism) non living (Marine, Rock, Mineral) sources. They can provide a skeleton (Template) for the design of new drug as a lead molecule<sup>1</sup>.

Since ancient time natural product are plays a crucial role in the human health due to the presence of medicinal agent. According to World Health Organizations (WHO) about 80% of world population depend upon the traditional medicine (nature obtained medicine) for the purpose of health care<sup>2</sup>.

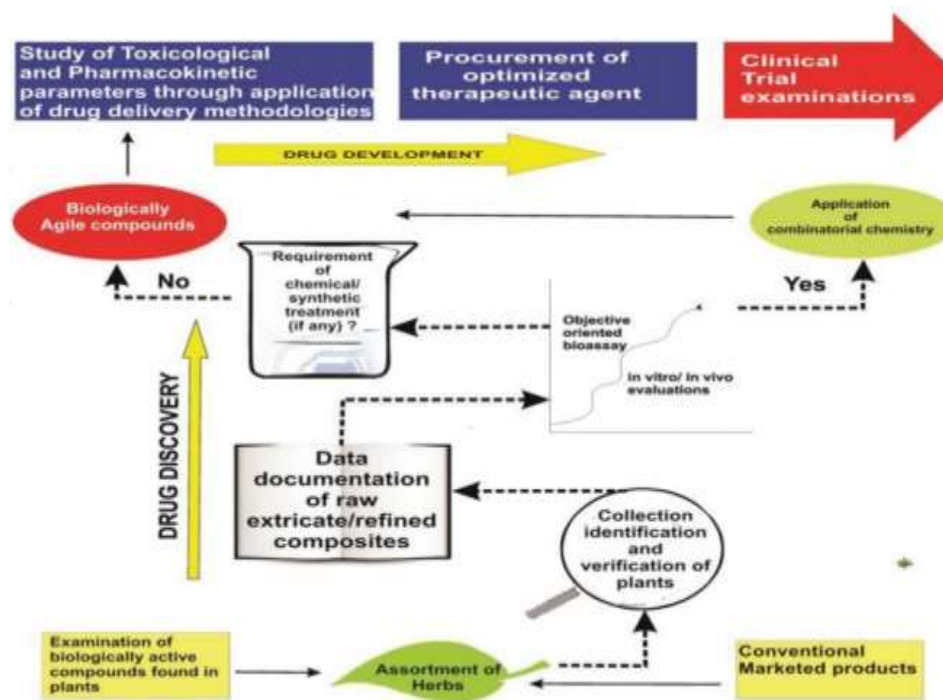


fig: Drug development process

The theory of drug- receptor action for the drug isolated from the Plant extract, lead a new era in the field of new drug discovery. In the modern medicine system a lot of medicine have been obtained from the natural sources such as Plants, Micro-Organism, Marine-Organism, and minerals.<sup>3</sup>

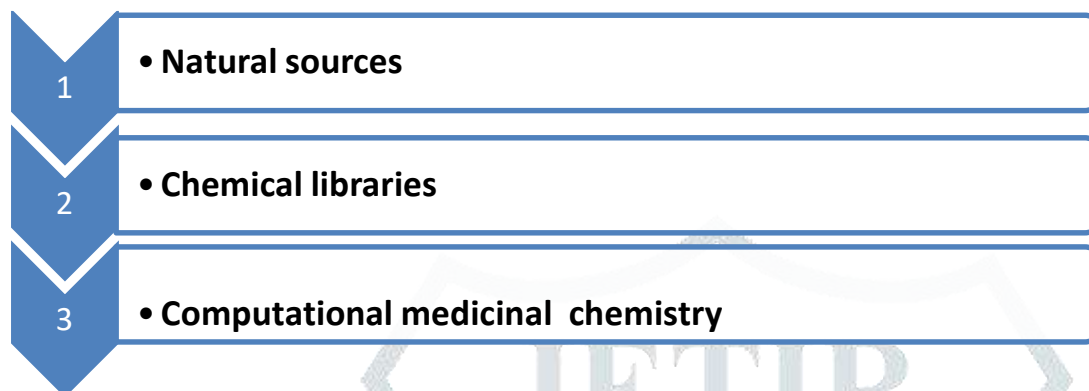
**Key words:-** Introduction, Lead compound, Drug, Natural product, Microorganism, Combinatorial chemistry,....

### Natural products as a new drug lead:

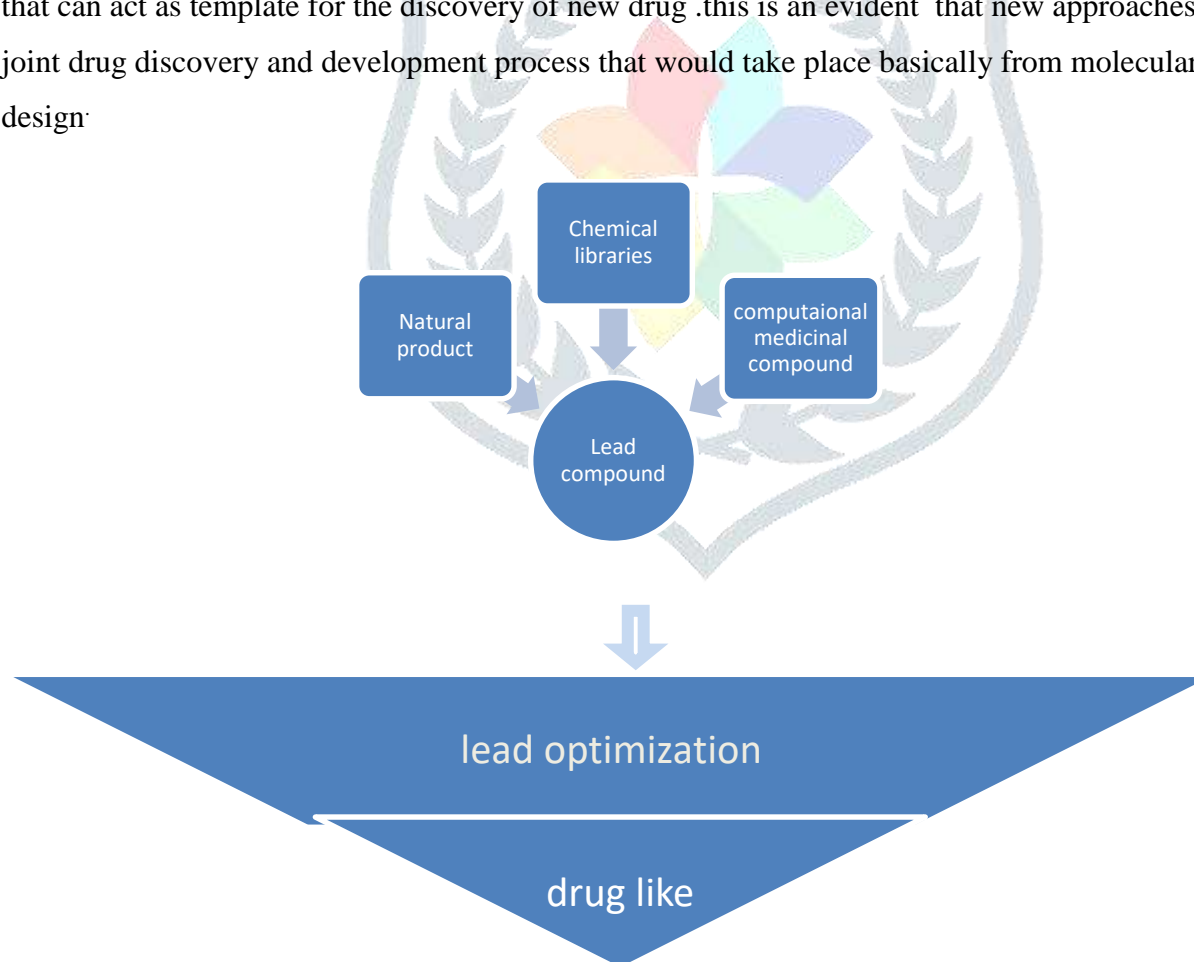
In the field of new drug development lead identification and lead optimization is a most important steps. By making certain structural changes in the structure of chemical compound, the pharmacological properties /drug efficacy, potency, selectivity and pharmacokinetic parameters are improved. The chemical structure of a compound play a crucial role in the lead identification process. The study of Absorption, Distribution, Metabolism, Excretion and Toxicological study of probable drug is the second step after lead identification. If the results are above studies are positive and satisfactory and the compound have non mutagenic and non

toxic effect than the compound is considered as a potential lead compound .this compound may then developed as new drug .

The lead compound is a starting molecule for new drug discovery ,the lead compound has desired pharmacological activity and may impart in the development of new drug molecule. There are some common sources of new lead compound and novel drugs are :-



The research based on Natural product care are continues for explore the variety of lead chemical structure that can act as template for the discovery of new drug .this is an evident that new approaches to enhance the joint drug discovery and development process that would take place basically from molecular insight of drug design



## Natural sources of drug

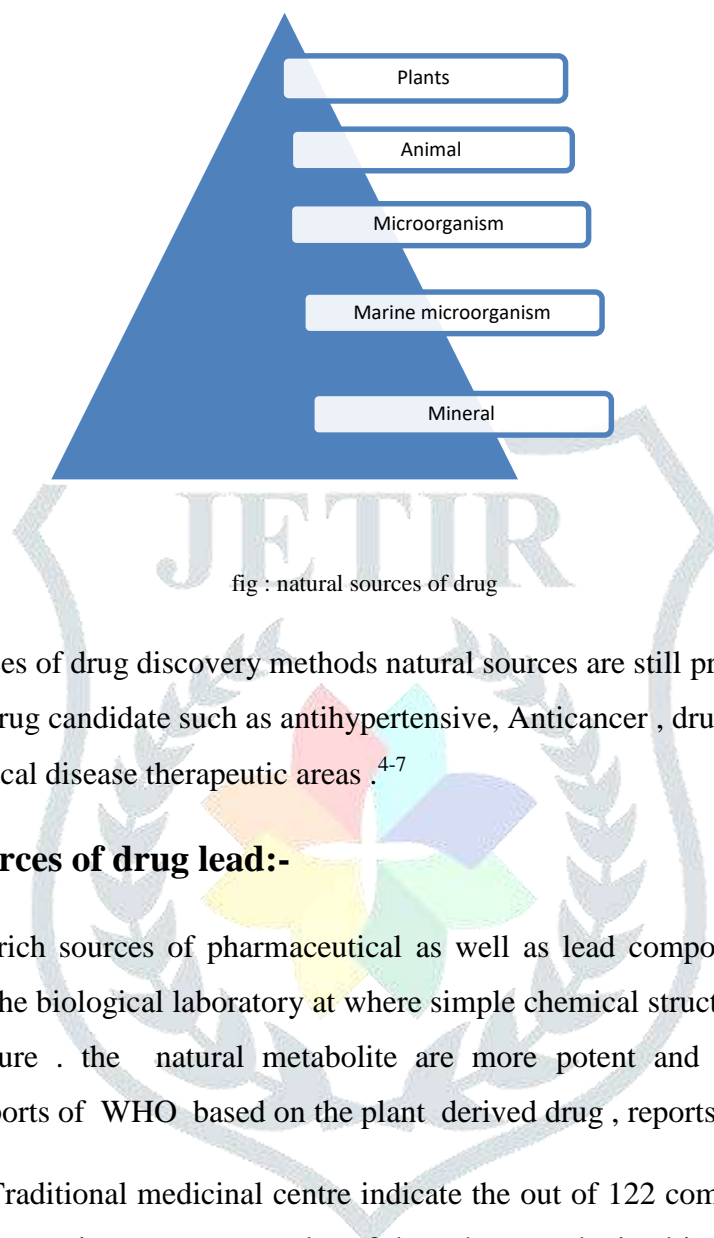


fig : natural sources of drug

In comparison of all sources of drug discovery methods natural sources are still providing a great share in the development of new drug candidate such as antihypertensive, Anticancer , drug Anti infective ,Immuno - supression and Neurological disease therapeutic areas .<sup>4-7</sup>

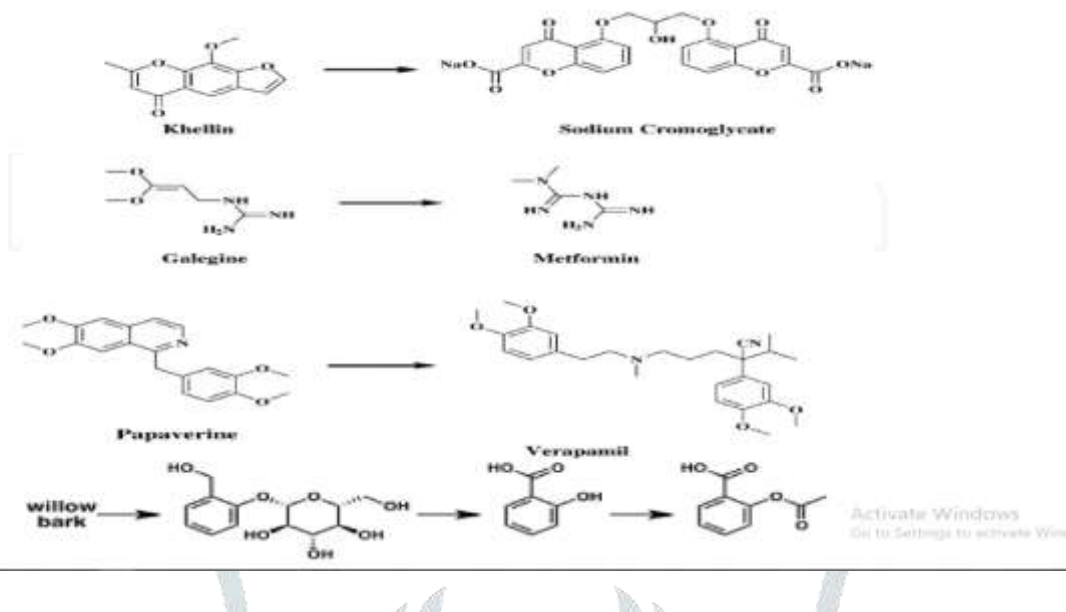
### Plants as natural sources of drug lead:-

Plants are consider as a rich sources of pharmaceutical as well as lead compound for drug development process . It is also called the biological laboratory at where simple chemical structure are transform in to the complex chemical structure . the natural metabolite are more potent and efficacious than synthetic molecules .In a survey reports of WHO based on the plant derived drug , reports that:-

Traditional medicinal centre indicate the out of 122 compound identified 80% were derived from the 94 plants species . some examples of drug that are obtained in this approach are : sodium chromoglycate , A bronchodilator drug from *khellin (Ammi Visnaga )* Metformin an antidiabetic drug from *Galigine(Galiga officinale )* Verapamil an antihypertensive drug *from Papaverine (Papaver somnifera)* ,Aspirin from *Salicine (Willow bark )* .

In 1820 a French pharmacist isolated an anti malarial drug *Quinine* from( *Cincona bark*), Quinine provide base for the synthesis for another common anti malarial drugs. Another antimalarial drugs developed from plant lead *Artemisinin* from *Artemisnin annua* .

Other drug developed from traditional medicinal plant are : *Reserpine* anti hypertensive drug from *Rauwolfia serpentina* and *Ephedrin* From *Ephedra sinica*, used as basis for the anti asthmatic drug *Salbutamol* and *solmeterol*..<sup>8</sup>



Phytocompound	Medicinal properties	Structure
Curcumin	Antibacterial, anticancer, antidiabetic, anti-inflammatory	
Morphine	Analgesic, Pain reliever	
Quinine	Antibacterial, Antimalarial	
Thymol	Antifungal, antibacterial dental care.	
Isobavachalcone	Antiplatelet, antioxidative, antitumor, neuroprotective, anti-inflammatory.	

### Animal as a source of drug lead :-

Amphibians , Reptiles, and human have been a good source of drug . Epibatidine is screened out from the skin of frog (*Epipedobates tricolor*) which are analgesic in nature ,that`s analgesic activity is much more than Morphine but main difficulty with it that the therapeutic dose is more close to the toxic dose ,thus epibatidine is turned out to be important lead compound for the synthesis of novel pain killer .

Antihypertensive drug Captopril (ACE inhibitor) are synthesized from the teprotide which are isolated from the venom of the snake pit viper (Bothrops Jararaca).

The Expandin -4 isolated from the venom of the Gila monster (*Heloderma suspectum*) that act for the synthesis of Byetta an injectable Antidiabetic drug use to control Type-2 diabetes mellitus.<sup>9</sup>

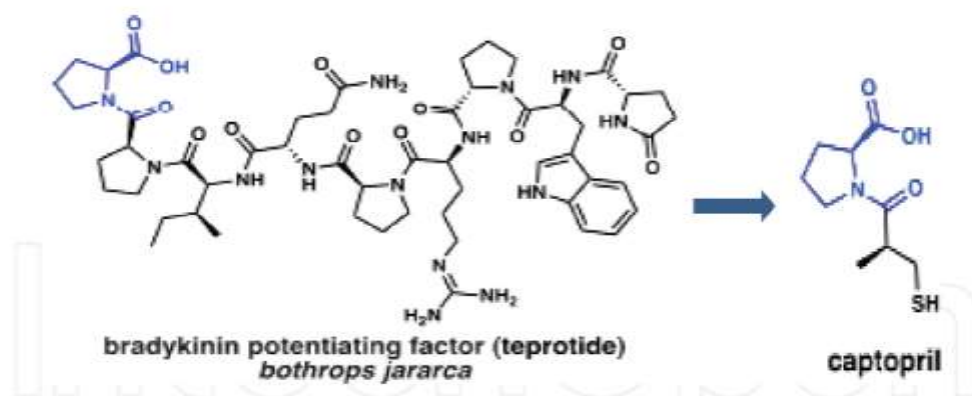


fig ;Drug from snake venom.

### Micro-organism as a source of drug lead :-

Alexander Fleming steers a new era in the field of medicine “Golden era of Antibiotic ” by the discovery of penicillin from *Penicillium notatum* in 1929 and boost up the investigation of nature for bioactive agent, Various Bioactive microbial metabolite turned in to the vital source of drug in pharmaceutical industries such as Penicillin from *penicillium notatum* and Cephalosporin from *cephalosporium acrymonium* and tetracyclin etc..

In addition to this Immuno-suppressive agent like Cyclosporin from *trichoderma*, Cholesterol lowering agent such as Mevastatin from *penicillium species* and Lovastatin from *Aspergillus species*, Antihelminthic and Antiparasitic agent Ivermectin from *Streptomyces species*.<sup>9</sup>

Examples of some anti-tumour drugs produced by micro-organism:-

Bleomycine	Streptomyces verticillus
Mitomycin	Streptomyces caepitocus
Daunomycin	Streptomyces peucetius
Doxorubicin	Streptomyces varcaesious

**Marine micro-organism as adrug lead :-** Seventy five percent of earth surface has been covered by water ,marine environment charecterises various diverse resources towards new drugs to fight most major disease like malaria and cancer .The aquatic organism are used for new drug development s mostly used for the new drug development mostly all over the world .thus under the marine pharmacology ,there is further scope for research on the basis of candidate drug's:-

- Genetically engineered marine organism.
- Manufacture of Pharmaceuticals and Nutraceuticals of marine origine .
- Chemical produced by or found in marine organism shown to have a wide variety of applications as Pharmaceuticals.<sup>10</sup>

**Natural product drug discovery and development: an integrative approach:-**An integrative approach comprising various discovery tools and novel discipline would definitely endow with an input in natural product drug discovery and development. Natural product can be envisaged to remain an indispensable component in the development of new drug. According to Lutz natural product not only complement synthetic molecule, they also exhibit drug-related features unsurpassable by any synthetic compound. An important attribute of natural product is their huge structure and chemical diversity. Another beneficial feature of natural product is their biological history. The natural products possess an inherent ability to interact with other molecules, which is a crucial precondition for making a drug.The natural product due to its sterically more complex structure exhibit advanced binding properly compared with synthetics. The natural products are perceived as “drug like-ness” and “biological friendliness” than totally synthetic molecule making them apposite lead candidates.The process of drug discovery involves the identification of candidates, synthesis, screening, characterisation and assays for therapeutic efficacy, which in fact is a very lengthy and tedious process. Considering the success of natural products as source of new drugs, new technologies have emerged to facilitate the process. These technologies are combinatorial chemistry, high throughput screening (HTS), bioinformatics, proteomics and genomics.

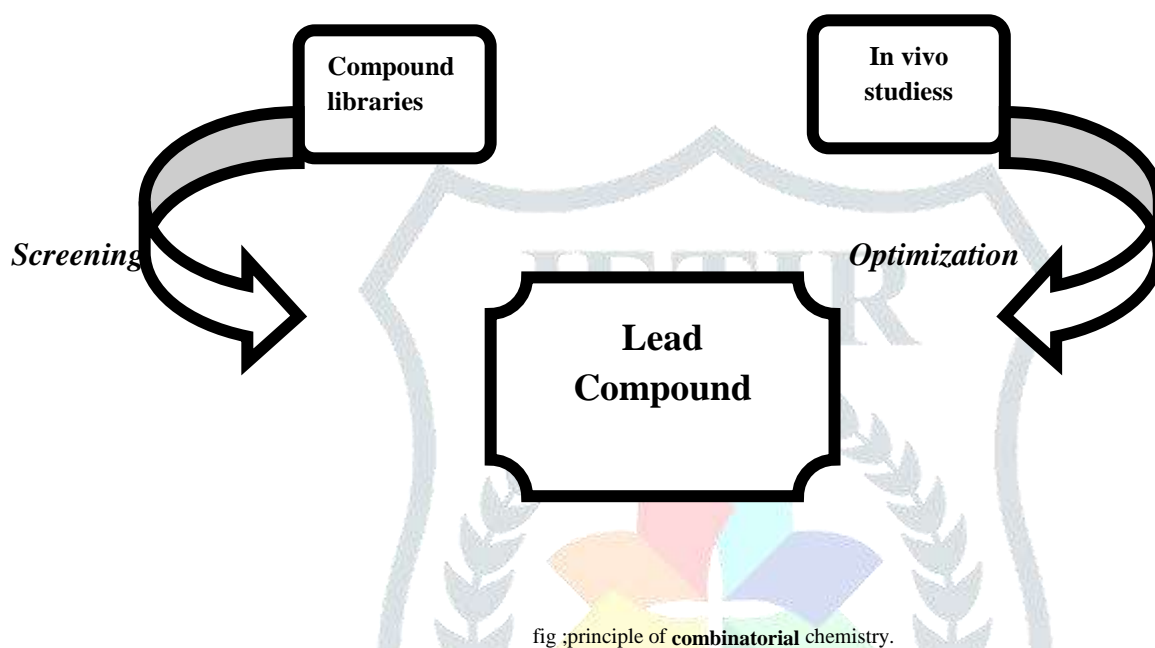
Other recently developed techniques are molecular diversity, compound library design,MMR based screening, QSAR and computer-aided drug design.

### **Combinatorial chemistry in drug design :-**

Combinatorial chemistry comprises the chemical synthetic methods that makes it possible to prepare a large number (ten to thousand or millions) of compound in a single process .combinatorial chemistry is mainly common in computer aided drug design and can be done online with web based software ,such as mole inspiration .

## Principle of combinatorial chemistry:-

It is a method through which large number of structurally distinct molecule may be synthesized at same time and submitted for pharmacological assay .The major advantage of this method are large range of analogue is synthesized using same reaction condition and same reaction vessels. By the application of this method the chemist can synthesized many hundred or thousand of compound in one time instead of preparing only a few by simple methodology.



## Challenges facing with natural lead compounds:-

The challenges in the new drug development from natural leads are mainly due to;-

- Existing prototype for drug discovery in large pharmaceutical Industries.
- Technical limitation of natural product .
- Increase steric complexity .
- Presence of large number chiral centers ,
- Ratio of aromatic rings atom to total heavy atoms ,that is low .
- Molecular rigidity is high .

## Conclusion:-

The discovery of drug from natural products are a new strategic option in the field of Pharmacy .Bioactive molecule from the natural products are screened out through various technique such as Combinatorial biosynthetic technique ,Microbial genomics and other screening process. This review made effort to introduce significance of natural product as bio-molecule also as Pharmaceutical agents.



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