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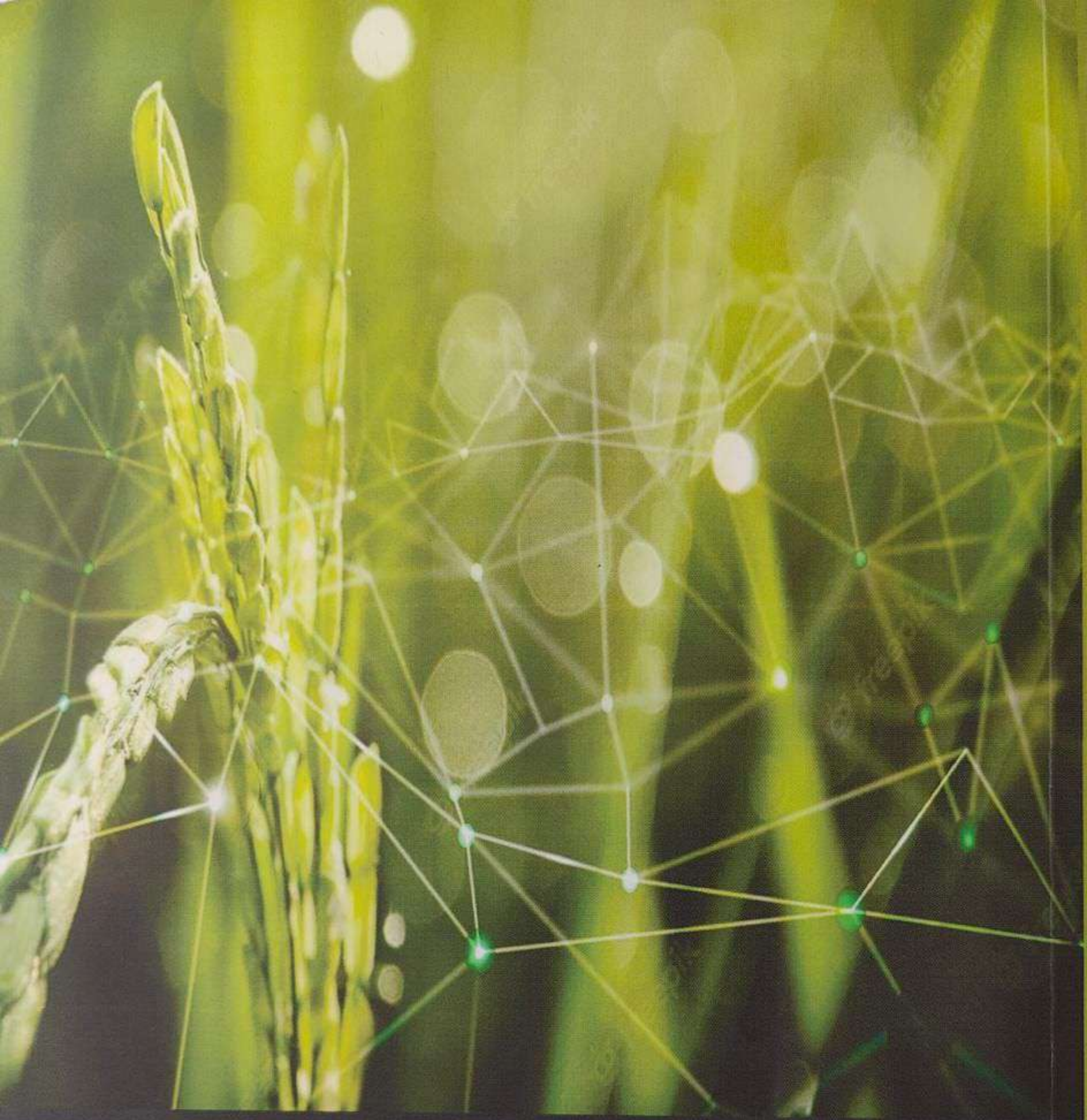

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Volume - 1

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And

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Chapter - 1

Phenolics & Alkaloids Based Phyto-Secondary Metabolites & Their Pharmacological Application

Anil Kumar Koshal and Sadiya Patel

Abstract

The comprehensive and multipurpose medicinal properties of phytopharmacophores of the plants are basically reliant on their phytochemical constituents. Commonly, the plant phytopharmacophores ingredients are classified into two classes based on their role in basic metabolic phenomenon, namely primary and secondary metabolites. Primary metabolite is a kind of metabolite that is directly involved in normal life functions such as growth, development and reproduction of the plants. It generally accomplishes a physiological function in the organism. It is also discussed as a fundamental metabolite; therefore, they are more or less similar in all living organism of the plants.

However, Secondary metabolites are ingredients that are not necessary for a cell organism to live, but play a vital role by the interaction of the cell organism with its environment. These constituents are regularly involved in plants protection against biotic or abiotic stresses.

In the sequence of perusal, the pharmacophore effects of herbals are concerned with the secondary plant metabolites. Secondary plant metabolites played an important role in diminishing several ailments in the traditional pharmacophore and mutual uses. In series of contemporary pharmacophores, they provided central ingredients for the production of drugs for treating various ailments from minor up to heart attack, cancer etc. Secondary plant metabolites are categorized according to their chemical structures into various groups and sub groups. In this chapter, we will be proposing numerous classes of secondary plant metabolites, their dispersal in diverse plant families and their pharmacological applications.

Keywords: phyto-secondary metabolites, alkaloids, phenolics and phytopharmacophore

1. Introduction

Throughout the ages, people have dependent on nature for their elementary needs, for the production of food from crops and fruit, accommodations, clothing, manures, flavours, fragrances and drugs for treating of various ailments. Plants play an important role in conventional as well as modern herbal Phyto-pharmacophores [1].

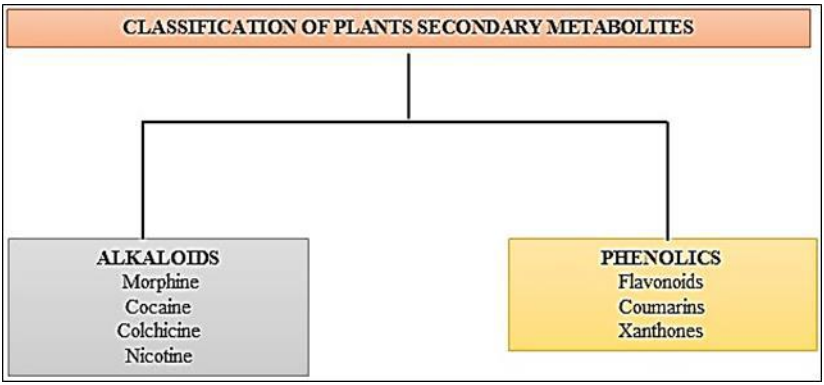
According to the WHO (Worlds Health Organization), any herb, plant, vegetable, which encompasses the ingredients that can be used for therapeutic purposes or which are precursors agents of pharmacophore, semi-synthetic new drug is referred to as medicinal plants [2]. Recently, there has been a transition in universal trend from synthetic to photochemotherapeutic, which can be said return to nature. Plant-isolated drugs have been a part of the evolution of human healthcare for thousands of years. Phytochemistry is the foundation of the chemotherapeutic uses of medicinal herbs [3]. A good knowledge of the composition of associate ingredients of medicinal plants leads to a better understanding of its possible therapeutic worth.

Metabolites are the end products of metabolic processes in plants and intermediates gradients formed during metabolic processes [4]. Phytochemistry has pronounced role of primary phytometabolites in elementary life functions such as cell development, growth, respiration and reproduction [5]. It includes the various components formed during different phenomena such as glycolysis, Krebs, photosynthesis and many associate path ways. Primary phytometabolites include small molecules such as carbohydrates, amino acids, starch, proteins, nucleic acids etc. In conclusion, the primary phytometabolites are similar in all alive cells of plants [6].

Secondary metabolites are not necessary as primary metabolites as these are not directly involved physiological and biological activity of plant cell. They are organic ingredients which are indirectly play a vital role in survival of plants but they produce some chemical ingredients which assist them in their physiological and biological growth and development [7]. Plant secondary metabolites are organic compounds biosynthetically produce from plant primary metabolites [8].

Plants secondary metabolites are known to possess various physiological and biological effects, which assign the scientific base for the use of medicinal plants in the traditional chemotherapeutic agents in many communities [9]. They have been described as antimicrobial and anticancer and many more activity against pathogen, therefore they are able to shield plants from pathogens. Besides, they prevent various stem, fruit and leaf to damage from the UV light [10].

Secondary plant metabolites are classified according to their chemical structures into a lot of categories. In this section, the nature of secondary plant metabolites will be deliberated as a foundation for a review of the main classes of constituents considered to be of therapeutic importance. Each section describes an overview of a class of the plant secondary metabolites concerning structure, botanical spreading in nature and generalizations about chemotherapeutic uses, followed by examples of representative secondary metabolites. The category of secondary plant metabolites include:



2. Alkaloids

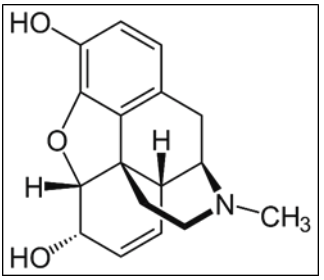
Alkaloids are primarily found in plants and generally in certain classes of flowering plants. In fact, one fourth of higher plants are assessed to contain alkaloids ingredients, among which numerous and different types have been identified [10]. They occur mostly in seed-bearing plants mainly in berries, bark, fruits, roots and leaves. Alkaloids often contain at least one nitrogen atom in heterocyclic ring. These are basic in nature and thus referred as alkaloid (alkali-like) [11].

Opium poppy (*Papaver somniferum*) and the ergot fungus (*Claviceps*) individually contain about 30 types of different ingredients of alkaloids. The Ranunculaceae, Solanaceae and Amaryllidaceae are other leading alkaloid-ingredients containing families. Ergot and few other fungi species also produce alkaloid [12].

Alkaloids are the important classes of secondary metabolites which are found to possess important biological properties like analgesic, muscle relaxant, antioxidant and many more [13]. These are used for the help of mankind and found beneficial for life-threatening diseases. Some important phyto-alkaloid described in this chapter are as follow:

2.1 Morphine

Morphine is the first alkaloid compound to be isolated and crystallized in 1804, was the potent active ingredient of the opium poppy, morphine [14]. The molecular formula for morphine and its hydrate form is respectively $C_{17}H_{19}NO_3$ and $C_{17}H_{19}NO_3.H_2O$, are less soluble in water or lipids. It is a benzyl isoquinoline alkaloid [15].

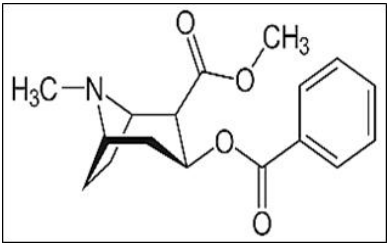


Opium poppy morphine

Morphine is used mainly to treat both acute and chronic severe pain. Its period of analgesia is nearby three to seven hours. It is used for the treatment of pain due to myocardial infarction and for labor pains also it is beneficial. Morphine has also been traditionally used in the treatment of acute pulmonary edema and effective in relieving cancer pain [16].

2.2 Cocaine

Cocaine is a naturally occurring stimulant Phyto-drug which is isolated from the leaves of the coca plant (*Erythroxylon coca*). Coca leaves possesses only about ½-1% cocaine. Chemically the molecular formula of cocaine is $C_{17}H_{21}NO_4$ and it is the ester of benzoylecgonine with methyl and is also known as 3β-hydroxy-1αH,5α-H-tropane-2β-carboxylic acid methyl ester benzoate [17].



Coca leaves cocaine

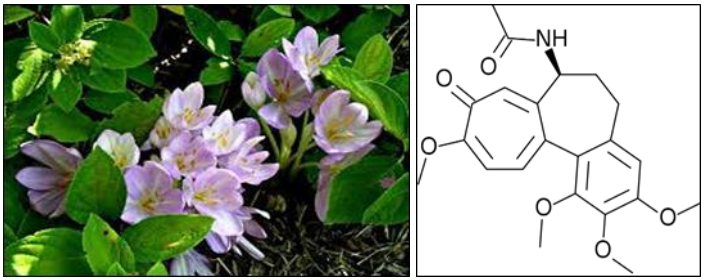
Cocaine is a tropane alkaloid with central nervous systems stimulating and shows local anaesthetic efficiency. Cocaine obstruct the dopamine,

serotonin and norepinephrine passage and prevents the re-uptake of serotonin, dopamine and norepinephrine into pre-synaptic neurons system [18]. This leads the way to aggregation of the respective neurotransmitters in the synaptic cleft and may result in improved postsynaptic receptor activation. Cocaine is a prescribed pharmacological drug used to treat the symptoms of Anaesthesia of the Nasal Cavity and Mucous Membrane. Cocaine may be used as pure drug or mix with other medications in constant percentage. Cocaine belongs to a class of medication known as local anaesthetics, esters [19].

2.3 Colchicine

One of the best known biologically active compounds from ancient times is colchicine, an alkaloid naturally occurring in *Colchicum autumnale* a plant of *Liliaceae* family and also in *Gloriosa superba*. It was isolated for the first time in 1820 from *Colchicum autumnale* plant (autumn crocus) [20].

Colchicine is an alkaloid compound possessing the molecular formula $C_{22}H_{25}NO_6$ and chemical name N-[(7S)- 5,6,7,9-tetrahydro-l, 2,3,10-tetramethoxy-9-oxobenzo(a)heptalen-7-yl)acetamide]. Colchicine contains three rings, A-ring which is trimethoxy phenyl ring), B-ring which is a saturated seven membered ring and C-ring which is tropolone ring.



***Colchicum autumnale* colchicine**

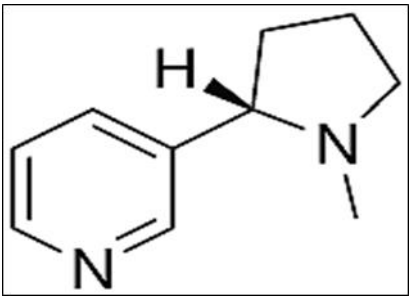
Colchicine is pharmacologically used to treat in gout and behçet's disease. In gout disease, it is less preferred to NSAIDs or steroids. At lower doses, it is well tolerated, in a review it was mentioned in low-quality evidence that low-dose colchicine reduced gout symptoms and pain both whereas high-dose colchicine was effective against only pain. Colchicine is also used as an anti-inflammatory agent for long-term treatment of Behçet's disease [21].

2.4 Nicotine

Nicotine, an organic phyto secondary metabolite compound that is the principal alkaloid of tobacco which is isolated from *Nicotiana tabacum* L. plant of solanaceae family, is a perennial herbaceous plant. Nicotine occurs

throughout the tobacco plant and especially big amount in the leaves. It is found only in cultivation, where it is the most commonly grown of all plants in the *Nicotiana* genus, and its leaves are commercially grown in many countries to be produced into tobacco [22].

Nicotine is also known as 3-(1-methyl-2-pyrrolidinyl)pyridine according to the IUPAC nomenclature. It is a bicyclic compound with a pyridine cycle and a pyrrolidine cycle with nitrogen as a heteroatom. The molecule possesses an asymmetric carbon and so exists in two enantiomeric compounds [23].



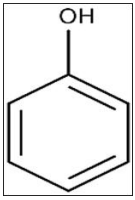
***Nicotiana tabacum* leaves nicotine**

Nicotine has been used as an pesticide and insecticide since at least the 1690s, in the form of tobacco extracts. But now days chemists have prospered in using genetically modified tobacco plants to produce drugs for several autoimmune and inflammatory ailments, comprising diabetes [24].

The primary chemotherapeutic use of nicotine is to treat addiction of nicotine by eliminating smoking habits and the reduces the damage it does to health. Controlled levels of nicotine are given to patients through gums, dermal patches, lozenges, inhalers or nasal sprays to dissuade them off their dependence [25].

3. Phenolics

Phenolic organic ingredients are plant secondary metabolites, which are formed in the shikimic acid of plants and pentose phosphate via phenylpropanoid metabolization. They bear six membered carbon aromatic rings, with one or more than hydroxyl substituents and range from simple phenolic molecules to highly polymerized compounds [26].



Phenol

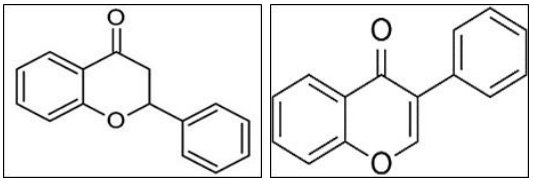
Phenolics compounds probably constitute the versatile group of phyto-secondary metabolites. They share the presence of one or more phenol groups as a common characteristic of phenolics and range from simple one aromatic ring to highly complex secondary plant metabolites ingredients [27].

They are widely available in various phyto families where they contribute significantly to the taste, colour and flavour of many herbs, foods and drinks. Some phenolics are preciouses chemotherapeutically for their anti-inflammatory activities such as quercetin or antihepatotoxic features such as silybin. Many of the phenolic molecules are also show antioxidants, especially flavonoids. Phenolics compounds can be broadly classified according to their structure or biosynthetic mechanism. According to their structures, phenolics can be classified into some simple phenolics. Some important of them such as flavonoid, coumarins, xanthones are pharmacological utility discussed in this chapter [28].

3.1 Flavonoid

Flavonoids are a large subgroup of plant secondary metabolites as phenolic ingredients compounds, widely available throughout various plants family and various prokaryotes species.

The general structure of flavonoids is a 15-carbon skeleton, containing 2 benzene rings connected by a 3-carbon linking chain 2-phenyl-1,4-benzopyrone is basic back bone of flavonoid this is also known as Isoflavan [29].



Flavonoid isoflavone

They represent various class of polyphenolic phyto-secondary metabolites ingredients with known chemotherapeutic activity. The flavonoid

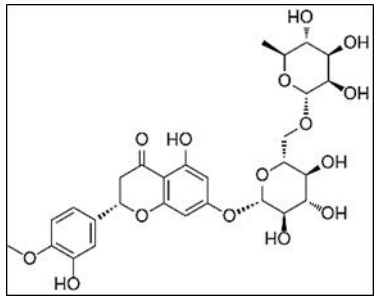
has also been described to exhibited other useful medication utility such as antiatherosclerotic, anti-tumour, antioxidant, coronary disorder, anti-micro pathogens and anti-inflammatory activities [30].

3.1.1 Hesperidin

In the series of various derivatise of flavonoids Hesperidin is an important organic ingredient of flavonoid isolated from citrus family lemon. Mainly hesperidin isolated from citrus fruits [31].

Chemically the name and molecular formula of hesperidin is respectively Hesperitin-7-rhamnoglucoside and $C_{28}H_{34}O_{15}$ and it is a yellow to brown powder with a molecular weight of 610.56.

Lemon fruit



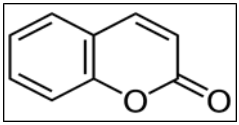
Hesperidin

A large number of citrus plant pharmacophore contain Hesperidin ingredients derivative of flavonoids, which have been isolated by many scientist as having anti-tumour, antibacterial, anti-fungal, anti-inflammatory, antiviral, antineoplastic, and heart disorder activity. Pharmacological effects are connected to antioxidant activity of hesperidin, appears through their ability to scavenge radicals. It has been reported to protect against DNA damage, lipid peroxidation [32].

3.2 Coumarins

Coumarins are secondary metabolites widely spread in nature, being found in green plants, fungi, bacteria, in some animal species, in fruits (bilberry, cloudberry), green tea and other foods and spices. Coumarin was first isolated from tonka beans in 1820 by A. Vogel [33].

Coumarin (1,2-benzopyrone, 2H-1-benzopyran-2-one, cis-o-coumarinic acid lactone) is a naturally occurring compound belonging to a large class of phenolic substances which present an aromatic ring fused to a condensed 6-member lactone ring. Coumarin is a colourless crystalline solid with a sweet odour resembling the scent of vanilla and a bitter taste [34].



Coumarin

Coumarin and Coumarin-related organic compounds have proved for many years having significant therapeutic potential in treating of various aliments arise due to various pathogens and other agents [35].

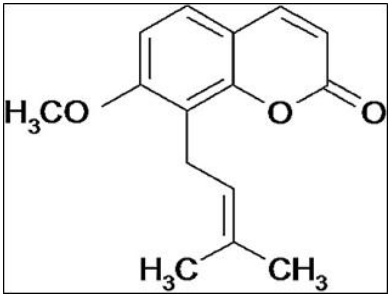
These are many important secondary plant metabolites which bearing classes of coumarin organic compounds. In the series of the coumarin containing secondary plant metabolites Osthole play an important role.

3.2.1 Osthole

Osthole, is a natural photo-secondary metabolites containing coumarin first time extracted from Cnidium plant. High content of Osthole is found the mature fruit of Cnidium monnieri, which is commonly applied in medical practice of Traditional Chinese Medicine, while it is also broadly found in other medicinal plants including Angelica, Archangelica, citrus etc. [36]

Chemically the name and molecular formula of osthole is respectively 7-methoxy-8-(3-methyl-2- butenyl)-2H-1-benzopyran-2-one and $C_{15}H_{16}O_3$.

Cnidium Plant



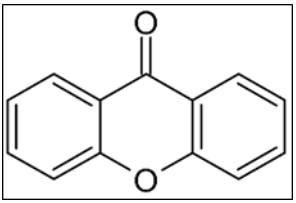
Osthole

Plenty of experimental results demonstrated that osthole exhibits a variety of pharmacological benefits including neuroprotection, osteogenesis, immunomodulation and cancer combating properties, making it a potential multitarget complementary medicine and functional food [37].

3.3 Xanthones

Xanthones are natural occurring polyphenols with the basic molecular formula $C_{13}H_8O_2$ that are commonly found in lichens, fungi and seven major genera of higher plants: Anacardiaceae, Gentianaceae and Guttiferae etc.

Chemically general structure of xanthone having three fused six membered aromatic ring in which centred ring bearing oxygen as a heteroatom.



Xanthones

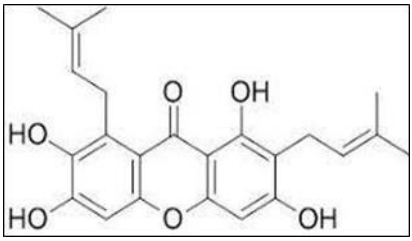
Plants belonging to the family Gentianaceae are known for their bitter taste due to the bearing of xanthones and are used in traditional remedies against loss of appetite and fever and are still included in many "tonic" preparation [38].

Xanthones isolated from natural sources are classified into six main groups, namely, simple xanthones, xanthone glycosides, prenylated xanthones, xanthonolignoids, bisxanthones and miscellaneous xanthones [39].

Xanthones are testified to give CNS stimulation and have strong hypoglycemic and anti-inflammatory activity. A crude extract of Swertia which bearing xanthones moiety has been assigned to insect repellent activity. In the series of Xanthone derivatise Mangostin is a important ingredients [40].

3.3.1 Mangostin

Mangostin is an important natural occurring plant-secondary metabolite of xanthones derivative. The main source of mangostin is Mangosteen (*Garcinia mangostana* Linn.) is a tropical plant from India, Myanmar, Malaysia, Philippines, Sri Lanka and Thailand. Mangostin isolated from the pericarp of mangosteen-fruit. Mangosteen *Garcinia mangostana* Linn commonly called "Queen of fruits and Food of Gods" [41].



Mangosteen fruit mangostin

In this chapter, medicinal assistances of mangosteen are categorized into numerous distinct areas including anti-cancer, anti-micro-pathogen and anti-

diabetes. Furthermore, its protection against damages and disorders in various humanoid organs such as liver, skin, joint, eye, neuron, bowel and cardiovascular tissues [42].

Conclusion

This chapter contains the importance of phyto-secondary metabolites organic ingredients from various plants species, with their classification, and pharmacological applications.

Since there is a persistent and crucial requirement for new medication agents to fight against tumour, cardiac aliments, cytotoxic, pathogen infectious diseases and autoimmune disorders of both animals and plants. The fight against any aliments is a vibrant symmetry between modern chemotherapy and natural selection on infectious or invasive agents. If the scientific circle is to put endless importance in this never-ending effort, then novel sources of bioactive phyto-secondary metabolites with new activities must be discovered. Phyto-secondary metabolites with noteworthy pharmacological activity are considered as an alternative to most of the synthetic pharmacophore and other commercially valuable components.

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Chapter - 2
Allergy and Antihistamine: The Significance of Medicinal Plants and Their Relevance in Drug Repurposing

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Chapter - 2

Allergy and Antihistamine: The Significance of Medicinal Plants and Their Relevance in Drug Repurposing

Dr. Shalini Nema and Dr. Shobha Shrivastava

Abstract

Allergic disorders encompass skin, food and respiratory allergies. Study present here includes plant metabolites like Polyphenols, Quercetin, Gossypin, Saponin, Steroidal lactone, alkaloids and many others are such class of compounds that are found in foods and plant sources and have been investigated for their anti-allergic, antihistamine and anti-inflammatory properties. These plants display their antiallergic potential through affecting mast cell, immunoglobulin, histamine and inhibiting different cytokines and interleukins. Research into repositioning known drugs to treat off target diseases other than the originally intended disease continues to grow and develop for therapeutic purposes. Phytoconstituents and the recent knowledge about SARS-CoV and SARS-CoV-2 pathology, profess their use in the prevention and management of COVID-19 pandemic. It is, therefore, believed to be an emerging strategy where existing plant metabolites having already been tested safe in humans, are redirected based on a valid target molecule to combat particularly, rare, neglected and difficult-to-treat diseases.

Aim: This review provides an overview of antallergic and antihistamine potential of respective plant extracts and also assess their use in drug repurposing against viral infections with focus on prevalent corona virus disease.

Keywords: Plant metabolites, Antiallergy, Antihistamine, Antiviral, Drug repurposing, SARS-CoV-2, Coronavirus.

Introduction

An allergy is an immune response, or reaction to substances that are usually not harmful. In someone with allergies, the immune response is oversensitive when it recognizes an allergens and induces the release of histamine. The substances that trigger the overreaction are called allergens.

The symptoms that result are called an allergic reaction. Histamine causes vessels to swell and dilate, leading to allergy symptoms.

The physiological mechanism of allergic reactions is the same in everyone. Allergens enter the body-either through ingestion, inhalation or contact with the skin or mucous membranes. This causes white blood cells to release an antibody which then binds to w mast cells. The mast cells rupture-and in the process, release biochemical substances including histamine.

Anaphylaxis and Allergen

Anaphylaxis is an allergic disease that occurs when the body is exposed to specific allergen. It could be caused by a variety of exogenous substances like allergens that include heterologous serum (such as tetanus antitoxin), certain animal proteins (such as that of fish, shrimp, and crabs), bacteria, viruses, parasites, animal fur, plant pollen, dust mites in the air, and chemicals and drugs. Allergens could stimulate human B cells to produce immunoglobulin E, which combines with antibodies on human mast cells and sensitized cells, damages the cell membrane and leads to degranulation, and releases histamine.

Histamine and its receptors

Histamine is synthesized and released by different human cells, especially basophils, mast cells, platelets, histaminergic neurons, lymphocytes, and enterochromaffin cells. It is stored in vesicles or granules released on stimulation. Histamine exerts its effects on target cells in various tissues by binding to its four receptors: histamine receptor $(HR)_1$, HR_2, HR_3, and HR_4.These receptors belong to the G protein-coupled receptors family (GPCRs) (Jutel, M. *et al*. 2005). H_1 receptor (HR_1) is codified in the human chromosome 3 and is responsible for many symptoms of allergic diseases, such as pruritus, rhinorrhea, bronchospasm, and contraction of the intestinal smooth. The presence of histamine stabilizes the receptor in its active form.

Antihistamines

Antihistamines are used in the management of allergic conditions. They are useful for treating the itching that results from the release of histamine. There fore, antihistamine are medicines that treat allergy symptoms by blocking the effects of histamine by stabilizing the inactive form of the receptor.

Mechanisms of action

Antihistamines are competitive inverse agonists at the H1 receptor that have preferential affinity for the inactive state of the receptor and stabilize it

in this conformation. Therefore, they are 'inverse agonists' that reduce the basal level of constitutive activity at histamine H1 receptors as well as blocking the agonist effects of histamine.

Antihistamines effects

1) Suppression of many of the vascular effects of histamine, with a reduction of vasodilation and oedema.
2) Inhibition of the accumulation of inflammatory cells in tissues.
3) Suppression of the immune response to antigens.

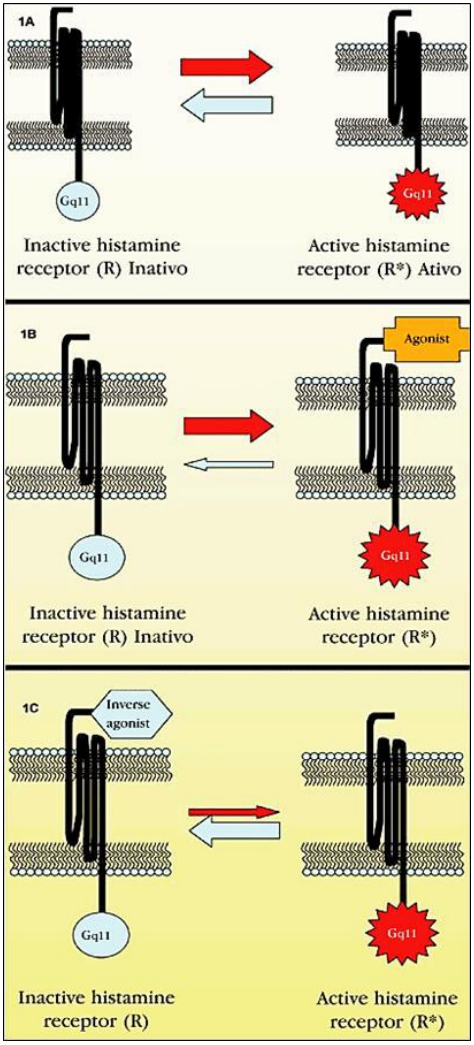

Fig 1: Mechanism of Action of active and inactivehistamine receptor

Importance of medicinal plants: A review

Plant-derived substances have recently become of great interest owing to their versatile applications. Medicinal plants are the richest bioresource of drugs of traditional systems of medicine, modern medicines, nutraceuticals, food supplements, folk medicines, pharmaceutical intermediates and chemical entities for synthetic drugs.

Antihistamine have many drawbacks including side effects of drowsiness and significant anticholinergic side effects. As a result, many patients with chronic allergic conditions, such as asthma, seek complementary alternative medicine (CAM) in order to achieve better control of symptoms. CAM is a set of healing resources that includes herbs that are used in traditional medicine (Slader, C.A. 2007). Bioactive natural products have played a key role in discovery of many important drug molecules and therefore medicinal plants are considered as potential sources a of new chemical entities (NCE) including viral drugs.

Singh, *et al*. (2011), highlight the presence of polyphenols in the daily diet confer them a safety profile and justifies their recognition as anti-allergic agents. It is known that polyphenols can form insoluble complexes with allergenic proteins changing their structure or rendering it less bioavailable.

Okunade, *et al*. (2004) have observed that plant alkaloids have considerable biological activity. They are known to have pharmacological effects and are used in medication.

Flavonoids are a class of natural product that is most extensively found in food associated with anti-allergic activity (Kempuraj, *et al*. 2005). On the other hand, saponins which are frequently found in several food plants such as soybeans, peas, spinach, quinoa, licorice, ginseng, capsicum peppers, eggplant and yam, present glucocorticoid-like activity and have huge biologic potential (Francis, *et al*., 2002).

Tannin contributes various medicinal properties such as antimicrobial, anti-inflammatory and astringent activity. They have been also reported to have anti-viral, antibacterial and anti-parasitic effect (Holvoet, *et al*. 2012).

Thymoquinone (TQ) is a chief bioactive constituent of black seed oil (Nigella sativa). TQ holds promising pharmacological properties against several diseases. It exhibits outstanding antioxidant, anti-inflammatory, anticancer, and other important biological activities, (Rahman, *et al*. 2020).

Drug Repurposing/drug repositioning

Drug repurposing is a process of identifying new uses for approved or investigational drugs and it is considered as a very effective strategy for drug discovery as it involves less time and cost to find a therapeutic agent in comparison to the de novo drug discovery process. Drug repositioning utilizes the combined efforts of activity-based or experimental and in silico-based or computational approaches to develop/identify the new uses of drug molecules on a rational basis. It is, therefore, believed to be an emerging strategy where existing medicines, having already been tested safe in humans, are redirected based on a valid target molecule to combat particularly, rare, difficult-to-treat diseases and neglected diseases.

Challenges

Drug repositioning is a complex process involving multiple factors such as technology, commercial models, patents, and investment and market demands. Another important issue is related to patent application and intellectual property rights (IPR). There are no provisions of IP protection of drug discovery by repositioning approach as per the IP and patent laws. For repositioned drugs, IP protection is limited (Rudrapal. M., 2020).

Significance and Benefits

This process do not require the initial processes of testing and approval thus saving time and resources. Most importantly, the already existing approved drugs have a known safety profile, which makes it an attractive proposition.

Drug repurposing has numerous advantages over conventional drug discovery approaches, including:

1) Considerably cuts research and development (R&D) costs.
2) Reduces the drug development timeline, as various existing compounds have already demonstrated safety in humans, it does not require Phase 1 clinical trials.
3) Potential for reuse despite evidence of adverse effects and failed efficacy in some indications.

Some popular drug repurposing approaches include

1) Repurposing oncology drugs.
2) Repositioning drugs across therapeutic areas.
3) **Aspirin:** Is a powerful drug that is not only being evaluated in the oncology field, but also in cardiac-related indications such as myocardial infarction.

4) Repurposing drugs to treat COVID-19: Drugs are also being repurposed as a treatment strategy against COVID-19, the disease caused by SARS-CoV-2. Several drugs are being evaluated including Lopinavir/ritonavir, Danoprevir plus Ritonavir and other combinations, Remdesivir etc.

Why phytoconstituents are a proven significant source?

Reasons

1) Demonstrate a broad spectrum of activity against pathogenic species.
2) Rarely have severe side effects.
3) Often possess the immunomodulatory action in humans.

Mechanism of action

Secondary Metabolites can affect the microbial cell in several different ways. These include the disruption of cytoplasmic membrane function and structure, interaction with the membrane proteins, interruption of DNA/RNA synthesis and function, destabilization of the proton motive force with leakage of ions, prevention of enzyme synthesis, induction of coagulation of cytoplasmic constituents, and interruption of normal cell communication ([Anand U. *et al*., 2019; Radulovic, *et al*., 2013). For example, Berberine (alkaloid group) from *Berberis* spp., can severely damage the structure of bacterial cell membranes and inhibit the synthesis of proteins and DNA under interaction with Streptococcus agalactiae.

Obviously, each compound that is extracted from a plant is not ready to be instantly used in routine clinical practice. We need antibacterial with sufficiently low inhibitory concentrations, minimal toxicity, and ease bioavailability for efficient and safe use in humans. Current advances in bio screening research, including the omics technologies, first of all metabolomics, will enable us to both catch and identify even very low-quantity active phytochemicals and clarify the specific molecular mechanisms underlying their effect(s) on bacterial targets (Cyrill. *et al*., 2020).

Ethnomedicinal plants: Their role in Antiallergy and Drug Repositioning.

Given below is a brief description of some potential ethnomedicinal plants which are known to exhibit anti allergic and antihistamine activity and are used in Chinese traditional system of medicine, Ayurvedic system, Unani

and as Prophetic medicines. These plants are explored further for drug discovery and repurposing drugs for other ailments. (Table: 1).

Methodology

The available informations on the medicinal plants which characterized antimicrobial potential were collected from electronic scientific databases: Pub Med, Science Direct, Scopus, Web of Science and Google Scholar. A total of 11 plants were included in the present review. Reviews from Various researchers regarding natural compounds from various medicinal plants were studied (Table: 1).

Table 1: Antiallergic Effects of Plant Species, Biological Response and reproposition

S. No.	Plants	Important phytoconstituents	Drug effect	Reference	Repurposing drug	Reference
1.	*Allium cepa, Malus domestica, Camellia sinensis and Fagopyrum esculentum.*	Quercetin (flavonoid)	Inhibition of histamine e release, decrease in pro-inflammatory cytokinesis suppressed interleukin IL-4 production.	Mlcek. J. *et al*., 2016	Against SARS-CoV-2	-Zhang D.H. *et al*., 2020 Lee H. *et al*., 2015
2.	*Hibiscus vitifolius* Linn	(Gossypin) Bioflavonoid	Inhibit antiprurities, systemic anaphylaxis reactions reduced the histamine release	Ganapaty S, *et al*., 2010	Against Herpes simplex virus	Lee j. *et al*., 1999
3.	*Aristolochia bracteolate* Lamk.	Chloroform extract	Mast cell membrane stabilization, Inhibiting histamine pathway.	Chitme *et al*. 2010	Broad spectrum of antibacterial activity	Negi, *et al*. 2003
4.	*Camellia japonica* L. Theaceae Leaf.	Ethanol	Degradation of mast cell	Lee J-H, *et al*., 2008	High antiviral activity on porcine epidemic diarrhea virus (PEDV) of corona virus family	Yang J.-L., *et al*., 2015
5.	*Camellia sinensis* (L.) O. Kuntze	Saponin	Decrease histamine level	Morikawa T. *et al*., 2007.	In various antivirus vaccines (saponin based adjuvants)	Sharma R. *et al*., 2020
6.	*Cordia verbenacea* D.C.	Sesquiterpene	Decrease edema	Fernandes *et al*., 2007	Antiviral activity on herpes simplex virus type 1 (Cordia salicifolia)	Hayasi K *et al*., 1990
7	*Withania somnifera* (L.) Dunal.	Steroidal lactone	Decrease the expression of IFN-IL-2 and decreases IL-4 level	Malik F. *et al*., 2007	Against SARS-CoV-2 S protein	Dhawam m. *et al*., 2021

8	*Azadirachta indica*	Nimbin (Triterpene)	Fungicidal, antihistamine and antiseptic properties.	Naik. M. *et al*., 2014.	Treatment for neurogenerative disease like Alzheimer's and Parkinson's disease, Type 2 Diabetes Mellitus and Polycythemia	(Dash *et al*., 2017)
9	*Solanum nigrum* L.	Alkaloid, cinnamic acid ester, steroid derivative (spirostan)	Degranulation of mast cell	Cai X-F, *et al*., 2010.	Anti-Hepatitis c virus v *et al*., Accine	Javed *et al*., 2011
10	*Glycyrrhiza uralensis*	glycyrrhizin	Antihistamines	Cao. w. *et al*. 2020	Against AIDS. (inhibit HIV replication).	Hatori. T. *et al*., 1989.
11	*Nigella sativa*	Thymoquinone (TQ)	Reducing the release of histamine and leukotrienes, anti-inflammatory.	Alsamarai A.M, *et al*., 2014	inhibit SARS-CoV-2 replication.	Rahman, M.T. 2020

Combating covid-19: Impact of antiallergic bioactive compounds on viral activity

Camellia sinensis* (L.) *O. kuntze

Saponin-based adjuvants selectively stimulate Th1 and cytotoxic T cell responses because they direct antigens into endogenous processing pathways and enhance IFN-γ release by dendritic cells. As a result, a robust antibody and cell-mediated immune response is activated. Therefore, more research is needed to develop saponin adjuvanted recombinant spike or RBD protein subunit vaccine. Development of a saponin adjuvanted subunit vaccine for SARS-COV-2 would also help us in tackling future pandemics associated with other novel coronaviruses (Sharma R. *et al*., 2020).

Withania somnifera

The medicinal attributes of W. somnifera are owing to a broad range of bioactive secondary metabolites including steroidal lactones [withanone, withanolide D, withanolide A, and withaferin A (WFA)]. Among these, WFA is one of the most interesting naturally occurring bioactive compounds that possess potent anti-tumorigenic, anti-inflammatory, pro-apoptotic, anti-angiogenic, and anti-invasive activities. WFA might bind to SARS-CoV-2 S protein and alter the S protein, thereby hindering its access into the host cells. Withanone and Withanoside V can impede the functional activities of SARS-CoV-2 main protease (Mpro). Withanolides have been found to control cytokine secretions during infection and could alleviate the cytokine storm in the lungs. The combined use of withanolides are several other drugs or therapeutic modalities, such as hydroxychloroquine and dexamethasone, has been demonstrated as an efficient strategy to improve the effectiveness of therapeutic regime for COVID-19 treatment (Dhawam. *et al*.,2021).

Glycyrrhiza uralensis

Licorice root (*Glycyrrhiza uralensis*) has shown strong antiviral activity. It was observed that extracted substance, glycyrrhizin sulphate, inhibit HIV replication, interfere with virus-to-cell binding and cell-to-cell infection, and induce IFN activity (Hatori. T. *et al*., 1989).

***Nigella sativa* (black seed)**

Nigella sativa could be considered for its bioactive components such as thymoquinone which was proven to have anti-viral activity. Further benefits to use N. sativa could be augmented by Zn supplement. Notably, Zn has been proven to improve innate and adaptive immunity in course of microbial infection. The effectiveness of the Zn salt supplement can be enhanced with

N. sativa as its major bioactive component might work as ionophore to allow Zn2+ to enter pneumocytes and inhibit SARS-CoV-2 replication by stopping its replicase enzyme system (Rahman, M.T. 2020).

Allium cepa, Malus domestica, Camellia sinensis* and *Fagopyrum esculentum

During the SARS-CoV-2 pandemic, Research based on molecular docking models with pharmacological network analysis for testing bioactive compounds have shown that quercetin from onions (Allium cepa), apples (Malus domestica), green tea (Camellia sinensis) and buckwheat (Fagopyrum esculentum) can inhibit the 6LU7 and 6Y2E proteases of SARS-CoV-2 by binding to them (Zhang D.H. *et al*., 2020 and Lee H. *et al*., 2015).

Cordia salicifolia extract

Partially purified extract from whole plant of Cordia salicifolia showed an inhibitory effect on herpes simplex virus type 1 (HSV-1). The activity of on different steps of HSV-1 replication in HeLa cells was investigated. Under single-cycle replication conditions, extract exerted a greater than 99.9% inhibition in virus yield. The extract has been shown to have a direct virucidal activity (Hayasi K *et al*., 1990).

Azadirachta indica

Nimbin (triterpene) has shown to have antipyretic, fungicidal, antihistamine and antiseptic properties. Also Nimbin is associated with anti-inflammatory and antioxidant effects, therefore reducing damage by mitigating the production of reactive oxygen species. Their metabolites found in Neem extracts are: limonoids, tannins, alkaloids, terpenoids, reducing sugar, catechins, sterols and gallic acid. Biochemical analysis done on leaf extracts has revealed high presence of proline, which is a current treatment for neurodegenerative diseases like Alzheimer's and Parkinson's disease, Type 2 Diabetes Mellitus and Polycythemia (Dash *et al*., 2017).

Solanum nigrum

Hepatitis c virus (HCV) infection is a serious global health problem necessitating effective treatment. Currently, there is no vaccine available for prevention of HCV infection due to high degree of strain variation. Methanolic and chloroform extract of Solanum nigrum seeds play a role in viral clearance during natural HCV infection. These data also suggest that therapeutic induction of extracts might represent an alternative approach for the treatment of chronic HCV infection or the present study leads to the

development of more potent and orally available HCV therapeutic drug (Javed *et al*., 2011).

***Hibiscus vitifolius* Linn**

The inhibitory effects of 12 flavonoids including gossypin against plaque formation of Herpes simplex virus type 2 (HSV-2) and 1 (HSV-1) was evaluated. It was found potent against HSV-1 and HSV-2 respectively (Lee j. *et al*., 1999).

Conclusion

Study here suggests that all the compounds and plants identified for allergy and antihistamine also showed antiviral potential when reproposed, hence unlocking a close relationship between ethnobotanical research and antiviral properties in plants.

Viruses can develop resistance through mutation to current antimicrobial agents, and this increases the need for the discovery and development of new effective compounds against old and new viral infections, especially against SARS-CoV-2. Secondary metabolites such as terpenes, flavonoids, alkaloids, saponins and stilbenes have been characterized through antiviral activity assays (Liu A. *et al*., 2012).

Plants secondary metabolites: Future perspectives

Research shows that some secondary metabolites of plants possess high-levels of intrinsic antimicrobial activity. However, it should keep in mind that, even in the case when a plant-derived substance reveals strong antibacterial, antifungal and antiviral effects, there is always the possibility that microorganism will appear to be non-susceptible or develop resistance to it. Therefore, a way to combine plant metabolites with conventional antibiotics might be the most profitable. Such combinations act at different target sites in bacterial cells and lead to high levels of efficacy, especially in suppressing the development of resistance. A detailed understanding of the molecular mechanisms underlying the action of phytochemicals, or of those underlying phytochemical-antibiotic interactions, is required for developing a successful therapeutic approach. The versatility of secondary metabolites and their low toxicity may provide novel antibiotics to tackle MDR (Multi-Drug Resistant) microbes too.

Today, advanced and rapid acting extraction, purification, and characterization techniques are needed for studying plant metabolites as well as multidisciplinary expertise and funding are very essential for novel drug discovery.

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Chapter - 3
Xylaria: The Natural Warehouse of Bioactive Potential Compounds in the Recent Past Decades

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Chapter - 3

Xylaria: The Natural Warehouse of Bioactive Potential Compounds in the Recent Past Decades

V. Ramesh, V. Siva and Dr. Kumari Sunita

Abstract

Xylaria is a large and the first described genus of the family Xylariaceae and reported to be promising and significant natural source of bioactive compounds. Bioactive novel natural compounds discovery and invention is a multidisciplinary endeavor that includes the search for new potent pharmaceuticals. *Xylaria* produce enormous diversified bioactive compounds with anticancer, antioxidant, antimicrobial, immune-stimulatory as a secondary metabolite via natural fruiting bodies as well as fermentation process and can be inexhaustible and sustainable resource. Researchers reported so far *Xylaria* as macro fungi as well as endophytic forms natural ware houses of biologically active compounds. Recent research and development technologies has opened new avenue on fungal research for highly sustainable and economically feasible novel natural products which are the frontiers of new drug invention. In this present review, we compiled the detailed reports of diverse class of novel secondary metabolites produced by the fungal species of *Xylaria* of its pharmaceutical importance.

Keywords: biological activity, endophytic *Xylaria*, macro fungi, novel natural products

Introduction

Nature has proven to be an endless source of abundant diversity of chemical entities with varying biological activities. The world health organization estimates that 80% of the world's population depends on traditional medicine for treating their everyday health problems. Natural products play a major role as active substances, model molecules for the discovery and validation of drug targets. Natural product researchers from fungal metabolite were revolutionized by the discovery of penicillin. It has factually saved millions of lives and sparked an era of fungal derived medicines (Tulp & Bohlin, 2004). This discovery of penicillin is still a front-

line antibiotic for some common bacterial infections, although its effectiveness is now limited by the development of drug resistant gram-negative bacteria. The phenomenal success of penicillin led to the intensive search for other antibiotic producing fungi.

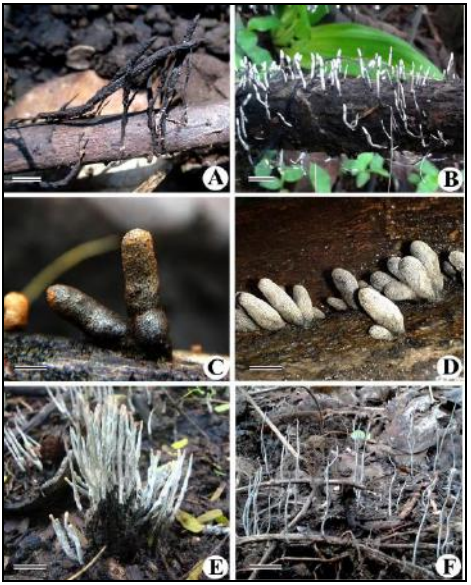
Plant kingdom harbors different kinds of microbes such as bacteria and fungi which are potent to producing biologically unique and diverse range of novel natural products (Rai *et al*., 2021). Fungi have been shown to be one source of a variety of useful natural products. They were common in nature and considered as good antimicrobial agents (Lindequist *et al*., 2005; Abad *et al*., 2007; Muhsin *et al*., 2011). As of 2010 approximately half a million natural products were known of which 60000-80000 are estimated to be of fungal origin. Approximately half of the latter display some kind of biological activity. Important discoveries other than antibiotics have included cyclosporine, an immunosuppressive drug used to prevent rejection of transplanted organs, produced by *Tolypocladium inflatum* (Hyde, 1996). The anticancer agent paclitaxel which was commonly known as taxol provides an interesting case. Initially it was thought to be produced solely from the bark of *Taxus brevifolia* Nutt, but it was later found to also be produced by the fungus *Taxomyces andreanae* (Katz, 2002; Strobel & Daisy, 2003). Macro fungi have been proved to be one of the most productive sources for producing a large and diverse variety of secondary metabolites with significant bioactivities (Mugdha *et al*., 2010). These are krestin from the cultured mycelium of *Trametes versicolor*, lentinan from the fruiting bodies of *Lentinus edodes* and schizophyllan from the culture fluid of *Schizophyllum commune* (Mizuno, 1993). Their previous successes in yielding useful natural products, their extensive habitat range and number of species yet to be discovered imply that fungi will continue to be a promising source of novel antibiotics. Endophytic fungal species are also recorded as natural ware house of potential bioactive compounds with pharmaceutical importances (Newman & Cragg, 2016).

The Xylariaceae is a large and relatively well-known ascomycete family found in most countries (Whalley, 1996) and it contains 35 genera (Eriksson & Hawksworth, 1993). It is characterized by perithecial ascocarps bearing paraphyses and periphyses that are embedded in a stroma. The asci of most species bear a ring at the apex that appears as a characteristic amyloid ascal plug when stained with iodine. Many species of *Xylaria* actively decay wood of living or dead angiosperms and are known to be saprobic in most cases (Rogers, 1979). They are saprobic or sometimes weakly to strongly parasitic on woody plants. Although they are found mostly on wood, some species are

found on sawdust, leaf and dung or soil. Moreover, Species of *Xylaria* living inside the plant tissues like stem, leaf and bark of both angiosperms and Gymnosperms as an Endophytic fungi (Boonphong *et al*., 2001). Families of Xylariaceae (for illustrations of representative species see Fig. 1, 1a & 1b) represented one of the most important and prolific lineages of secondary metabolite producers among the fungal kingdom (Becker & Stadler, 2021). In this review, we divided this into two major parts, the first one is dealing with isolation & identification and second the part consists of interesting novel bioactive compounds from the large genus of *Xylaria* of the family Xylariaceae.

a) *X. melanura* b) *X. telfairii* c) *X. grammica* d) *X. primorskensis* e) *Xylaria* sp. (JF795290), f) *X. curta* (JF795289) g) *Xylaria* sp. (KC405623) h) *X. digitata* & i) *X. persicaria* (Kevin Becker & Marc Stadler 2021); (Mohd Adnan *et al*., 2018); (Ramesh *et al*., 2012)

Fig 1: Fruiting bodies of some species of *Xylaria*



a) *X. apiculata* b) *X. carpophila* c) *X. cubensis* d) *X. curta* e) *X. feejeensis* f) *X. filliformis* (Koyani *et al*., 2016)

Fig 1a: Fruiting bodies of some species of *Xylaria*

a) *X. gigantea* b) *X. longipes* c) *X. nigripes* d) *X. polymorpha* (Koyani *et al*., 2016)

Fig 1b: Fruiting bodies of some species of *Xylaria*

Isolation and Identification

Isolation of *Xylaria* as a macro fungus

The fruiting body or stromata of the *Xylaria* spp. was washed thoroughly with sterile distilled water and was thereafter aseptically broken with aid of a sterile forceps. A small piece of 2×2 mm of the fruiting body was aseptically transferred onto plates containing PDA with 50 µg/mL of streptomycin to suppress bacterial growth. The plates were incubated at 30 °C for three weeks for the development of fruiting body (Fig. 2). The fungi growing out from the fruiting bodies were subsequently transferred onto fresh PDA plates without antibiotics (Ramesh *et al*., 2012).

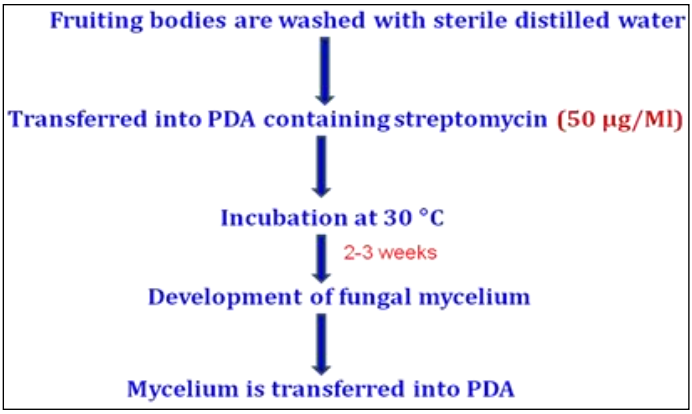


Fig 2: Graphical representation of mycelial cultivation macro fungal species of *Xylaria*

Isolation of *Xylaria* as an endophytic fungus

Commonly *Xylaria* sp., which are common endophytic inhabitants of most tropical plants, have been previously investigated for their production of new metabolites and have proven to be a good source of bioactive compounds (Espada *et al*., 1997). For isolation of endophytic fungi, any one of the asymptomatic healthy plant materials such as stem, leaf and bark were thoroughly washed in running tap water, and then it is surface sterilized by a slightly modified standard protocol of Raviraja (2005). The selected plant tissue were immersed in 95% ethanol for 30s, 4% sodium hypochlorite solution for 60s and 95% ethanol for 30s followed by rinsing with sterile distilled water three times for 10s and allowed to surface dry under sterile conditions. After drying, each plant material segment was cut into approximately 0.2-0.5cm squares and placed on Petri plates containing basic fungal culture medium such as potato dextrose agar medium (PDA)

supplemented with streptomycin (100 mg/L) to suppress bacterial growth. Petri plates were sealed with cling film and incubated at 30 °C in a light chamber for up to one week. They were monitored every day for growth of endophytic fungal colonies. Fungi growing out from the samples were subsequently transferred onto fresh PDA plates. The procedure of transferring to fresh PDA plates was carried out several times in order to isolate pure colonies (Fig. 3). Morphological characteristics such as size, shape and color of the fruiting bodies allow the identification of the fungal species of *Xylaria* (Sutton and Cundell, 2004) and it was reinforced by molecular confirmed by rRNA sequence comparisons (Altschul *et al.*, 1990).

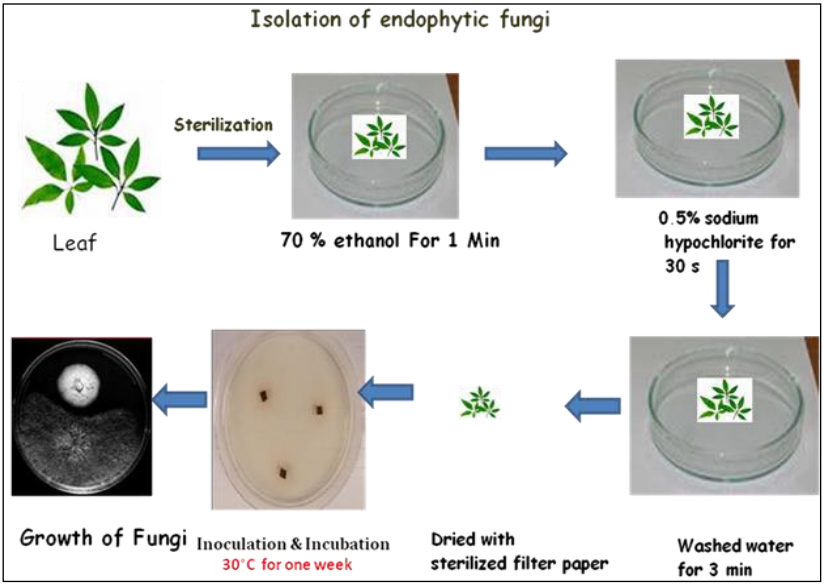


Fig 3: Graphical representation of Isolation of Endophytic *Xylaria*

Screening of bioactive novel natural products

Owing to the fungal bioactive metabolic unique versatility, ecological diversity and essential role in nature, fungi have been attracted the attention of various interdisciplinary researchers such as biologists, chemists, biochemists, geneticists, ecologists and naturalists in myriad ways (Tkacz & Lange, 2004). The use of *Xylaria* species for the production of pharmaceutically important products has a long tradition, but it has increased rapidly over the past half century (Papagianni, 2004). Secondary metabolites from the genus of *Xylaria* have broad spectrum of biological activities. Since the discovery antibiotic agent penicillin from *Penicillium* (Fleming, 1929), interest to find bioactive compounds from fungal genus has increased

considerably. Many important secondary metabolites that are potential leads for treatment of human diseases such as antioxidants, antimicrobial agents, immunomodulatory agents and anticancer agents, *etc*., have been identified from this genus (Song *et al*., 2011; Wu *et al*., 2011; Ko *et al*., 2009; Yin *et al*., 2011).

Xylaria as a source of anticancer agents

Based on the report of world health organization, 80% of the world's population predominantly in the developing countries rely on plant based natural products as therapeutic agent for the health care (Gurib-Fakim *et al*., 2006). Bioactive Natural products and their derivatives represent one of the important and more than 50% of all the drugs in clinical use of the world. Almost 60% of the drugs approved for cancer treatment are of natural origin. Moreover, as per the research report says that, more than 70% of the anticancer and antimicrobial bioactive compounds were derived from fungal origin (Newman & Cragg, 2020).

In the unremitting search for novel bioactive compounds from the species of *Xylaria* led to abundant natural products with bioactivities. In the Table 1, xylarichalasin A from endophytic *Xylaria* sp. isolated from roots of *Damnacanthus officinarum* showed the strongest activity against human cancer cell lines MCF-7 with IC50 value of 6.3 μM and SMMC-7721 with IC50 value of 8.6 μM (Wang *et al*., 2020). Likewise, cytochalasans derivatives from solid-state rice fermentation extract of *X. longipes* was reported by Wang *et al*., (2019). It is a novel compounds and exhibited cytotoxicity of IC50 > 40 μg/mL against human cancer cell lines like HL-60. Noppawan *et al*., (2020) reported and cultivated wood decaying macro fungal species of *Xylaria*. It has also cytochalasin named cytochalasin (Fig. 4) found to be active against HeLa cells (IC50 57 μg/mL), HT29, HCT116, MCF-7 (IC50 90 to >100 μg/mL). Similarly, curtachalasins A and B are bioactive cytochalasans from xylariaceae were found in the species of endophytic *Xylaria* cf. *curta* isolated from the potato stem tissue. These metabolites have promising bioactivities in its initial screenings for cytotoxicity and antimicrobial activities (Wang *et al*., 2018). A patent was published and dealing with a macrolide compound of clonostachydiol from *X. curta*, which showed cytotoxic effects against several human cancer cell lines (Ai *et al*., 2018). It was also the same compounds were isolated and reported from the *Xylaria* sp. and exhibited moderate cytotoxicity against diverse human cancer cell lines like HL-60 and A-549 with IC50 values of 4.9 and 25.6 μM, respectively (Ojima *et al*., 2018). Selective cytotoxic of a novel cytochalasin was isolated from a marine-derived *Xylaria* sp. and

named cytochalasin P1 (Fig. 4). It is chemically know as 19, 20-epoxide of the known cytochalasin P. It has significant cytotoxicity against human tumor cell lines like SF-268 and MCF-7 with the IC50 values of 1.37 and 0.71 μM (Chen *et al*., 2017).

Moreover, Ramesh *et al*., (2015a, & 2015b) studied and reported significant antitumor activity of both natural fruiting bodies and cultural filtrate crude extract as well as partial purified fraction against human cancer cell lines such as MDA-MB-231 (Breast carcinoma cells), A549 (Lung carcinoma cells) and MCF-7 (Breast carcinoma cells). Wei *et al*., (2015) isolated bioactive cytochalasins C, D and Q from the *Xylaria* sp. NC1214, a fungal endophyte of the moss *Hypnum* sp. (Table 1). They have investigated for their cytotoxic activity against five tumors cell lines. Among the above cytochalasins, cytochalasin D showed significant cytotoxicity against all five cell lines, with IC50s ranging from 0.22 to 1.44 lM, whereas cytochalasins C and Q exhibited moderate, but selective cytotoxicity. Isaka *et al*., (2011) isolated novel cytotoxic compounds of three new sesquiterpenoids and a new pimarane-type diterpenoid from the fermentation broth of the wood-decay fungus *Xylaria* sp. BCC 5484. Similarly, Yin *et al*., (2011) studied the cytotoxic activities of the compounds isolated from *X. carpophila*. These chemical compounds such as cyclopeptide cyclo (N-methyl-L-Phe31 L-Leu-D-Ile-L-Val), five new sesquiterpenes named as xylocarpus A-E and another known compound had cytotoxicity against human cancer cell lines. These compounds showed an effective antiproliferative activity. Moreover, earlier reports revealed that the novel anticancer compound of cytochalasins was extracted from the species of *Xylaria* (Pongcharoen *et al*., 2007; Rukachaisirikul *et al*., 2009; Zhang *et al*., 2010). Shiono *et al*., (2009) reported the cytotoxicity of the isopimarane diterpene glycosides extracted from the fruiting bodies of the ascomycete *X. polymorpha*. IC50 value of the compound ranged from 71 to 607 μM.

Table 1: Some of the reported bioactive natural products isolated from endophytic *Xylaria*

Bioactive Compounds	**Name of the species**	**Host Plants**	**Bioactivity**
Xylarichalasin A	*Xylaria* sp.	*Damnacanthus officinarum*	Anticancer Activity
Curtachalasins A and B	*X*.cf. *curta*	*Solanum tuberosum*	Cytotoxicity & Antimicrobial activities
Cytochalasins C, D and Q	*Xylaria* sp. NC1214	*Hypnum* sp.	Cytotoxicity

Ethyl acetate extract	*Xylaria* sp.	*Mussaenda luteola*	Antioxidant activity
Methanol extract	*X. feejeensis*	*Tectona grandis*	Antioxidant activity
Pentapeptides	*Xylaria* sp.	*Sophora tonkinensis*	Antibacterial activities
Xyolide	*X. feejeensis*	Amazonian forest plant	Antifungal activity
Proline containing cyclopentapeptides	*Xylaria* sp.	Endolichenic	Antifungal activity
Xylaria diterpenes A–R	X. *longipes*	*Fomitopsis betulina*	Immunosuppressive activities

***Xylaria* as a source of Antioxidants agents**

Among the many bioactive secondary metabolites recovered from the kingdom fungi, natural products that possess antioxidant potential occupy a major proportion. Antioxidants are compounds that obstruct free radical reactions and slow down cellular deterioration. Mohd Adnan *et al*., 2018 reported that the pharmacological properties of a potent and major bioactive compound like xylaranic acid from *X. primorskensis* (*X. primorskensis*). The terpenoids nanoparticles from xylaranic acid showed significant antioxidant potential against DPPH & H_2O_2 radicals and also its showed antibacterial and anticancer activity against human bacterial pathogens and human lung cancer cells. Rupesh D Divate *et al*., (2017) studied the Protective effect of medicinal fungus *X. nigripes* mycelia extracts against hydrogen peroxide-induced apoptosis in PC12 cells. They reported that, ethanol extract showed higher antioxidant activity by scavenging DPPH radicals, inhibiting lipid peroxidation, and reducing power. Hence, they said that, the macro fungal species of *X. nigripes* has high phenolic content and antioxidant activity may provide the neuroprotective effects. In the same year, Shylaja *et al*., (2017) studied and reported that the ethyl acetate extract of endophytic fungal species of *Xylaria* showed moderate antioxidant activity when compared to other endophytic fungal isolates isolated from *Mussaenda luteola.* Similarly, Durga & Rajagopal (2016) reported the methanol extract of *X. feejeenis* exhibited high antioxidant potential compared to ethyl acetate and chloroform extracts. They also studied the optimization of antioxidant potential of *X. feejeensis* by the statistical optimization by Plackett-Burman design and Central Composite Design. In this method, they found the increased antioxidant yield of *X. feejeenis* by 23%-75%. Fernando *et al*., (2016) investigated and reported that the antioxidant properties of terrestrial *X. feejeenis* harvested from the dry zone forest reserves in Dambulla and Mahiyanganaya areas of Sri Lanka for the first time. That species also exhibited a strong antioxidant capacity and high contents of phenolic and

flavonoid substances implying that studied forms possess an effectual antioxidative system.

Moreover, Liu *et al*., (2007) investigated the antioxidant activity of cultivated fruiting bodies of *Xylaria* sp. The results revealed that the methanol extract exhibited strong antioxidant activity in both DPPH and β-carotene-linoleic acid model system. Total phenolic and flavonoid contents were also highest in methanol extract of fruiting bodies. The results showed that total phenolic and flavonoid contents were the highest in methanol extract (54.51±1.05 mg gallic acid equivalent/g dry weight and 86.76±0.58 mg rutin equivalent/g dry weight), while the hexane extract was the lowest (9.71±0.57 mg GAE/g dw and 10.14±0.76 mg RE/g dw, respectively). Furthermore, the spectroscopic studies revealed that the extract of *Xylaria* sp. had bioactive compounds like esters, phenolics, alkanes, carboxylates and alcohols.

Xylaria as a source of immunomodulatory agents

Immunomodulators are the group of chemical substances that help to regulate and boost the immune system. The basic mechanisms by which the natural products of fungal species defend the body against infection caused by microorganisms have two probable ways one by destroying pathogens and other by enhance by stimulating the body immunity. In clinical practice, they are usually classified into three categories such as immunosuppressants, immunostimulants, and immunoadjuvants (El Enshasy & Hatti-Kaul 2013). Their market share has increased day by day rapidly in recent past due to wide-ranging pharmaceutical applications for patients that require human immune system modulations. They are also widely used as a prophylactic medicine for an increasing number even in healthy people (Reis *et al*., 2017 & Himanshi *et al*., 2017). However, most immunomodulators are in market were synthetic or semi-synthetic compounds, there has been a growing interest in natural immunomodulators. Indeed, most of the currently used chemical immunomodulatory drugs have negative side effects and the market share of natural immunomodulators is increasing rapidly with an annual growth rate of 8.6% (Shukla *et al*., 2014).

Recently, Chen *et al*., (2020a & 2020b) isolated *Xylaria diterpenes* A-R and two isopimarenes designated xylarilongipins A and B from the fungicolous species of *X. longipes*, growing on fruiting bodies of the basidiomycete *Fomitopsis betulina*. These both terpenoids products showed immunosuppressive activities against cell proliferation of concanavalin A-induced T-lymphocytes and LPS-induced B-lymphocytes. Rupesh D Divate

& Yun Chin Chung, (2017) studied the i*n vitro* and *in vivo* assessment of anti-inflammatory and immunomodulatory activities of hot water and 70% ethanol extracts of *X. nigripes* mycelium. They reported that, both the extracts effectively reduced the concentration of NO, TNF-α and IL-6 in culture medium, and Cox-2 enzyme activity. The phagocytic activity of RAW264.7 cells was enhanced upon treatment with *X. nigripes* extracts for 24 h. *X. nigripes* extract exhibited increased anti-inflammation effects, phagocytic activity, and secretion of anti-inflammatory cytokine IL-10. The *X. nigripes* mycelium exhibited immunomodulatory activities by enhancing splenocytes proliferation, cytokine inductions, and the cytotoxicity of splenic natural killer cells. Ko *et al*., (2011) investigated that the immunomodulatory properties of *X. nigripes* in peritoneal macrophage cells of Balb/c mice. The hexane and methanol extracts showed a dose dependent inhibitory effect on NO, PGE2, IL-1β, IL-6, TNF-α and IFN-γ production in LPS-stimulated macrophages. RT-PCR assay also showed that hexane extract possessed a greater inhibition than ethanol extract on iNOS and COX-2 RNA expression. Furthermore, hexane extract also showed a significant suppression effect than ethanol extract. Finally, these results conclude that hexane extract possessed a stronger anti-inflammatory activity than ethanol extract.

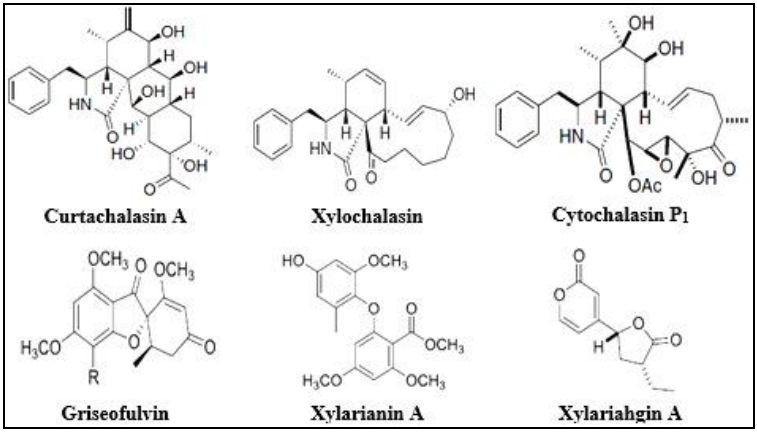
Similarly, Liu *et al*., (2006) studied the immunomodulatory effect of *X. hypoxylon*. They reported that lectin of *X. hypoxylon* (XHL) showed the excellent Inhibition proliferation of HepG2 cells. Likewise, *X. nigripes* (*Koltz.*) SACC. also known as wu ling shen, is a high value medicinal fungus belonging to the family of xylariaceae. It is found growing in wilds around the abandoned termite nests. In traditional Chinese medicine, it is known to enhance immunity and hematopoiesis (Xu, 1997). Moreover, the wild *X. nigripes* was also used for treatment of insomnia, trauma and as a diuretic and nerve tonic (Dai & Yang, 2008).

Xylaria as a source of Antimicrobial agents

The accelerating haunt for new antimicrobial drugs to provide assistance in medical community to combat drug resistance microorganism, the appearance of life-threatening bacteria, and the tremendous increase in the incidence of fungal infections in the world's population. Devaraju Rakshith *et al*., (2020) studied the antimicrobial potential of culture broth of *Xylaria* sp. FPL-25(M) against human bacterial and fungal pathogens by bioactivity guided fractionation using bioautography and chromatography. The isolated xylobovide-9-methyl ester exhibited broad-spectrum antimicrobial activity. Similarly, Yu *et al*., (2019) isolated and reported two known compounds of penixylarins C & D from the fungal species of *Xylaria* under axenic

condition. Its bioactivity exhibited against *Mycolicibacterium phlei* with the minimum inhibitory concentrations of 6.25 µg/mL and 12.5 µg/mL against *Vibrio parahaemolyticus*. Liang *et al*., (2019) isolated a number of antibacterial compounds, including a new eremophilane sesquiterpenoid named xylareremophil, from a *Xylaria* sp. it exhibited weak antibacterial activity with the minimal inhibitory values of 25 µg/mL against *Micrococcus luteus* and *Proteus vulgaris*.

Occurrence of antibacterial metabolites was reported from *Xylaria* sp. within two publications: in the first work (Zheng *et al*., 2018a), a new pyranone, 6-heptanoyl-4-methoxy-2H-pyran-2-one, was reported, while the second publication gave account on a novel phthalide named xylarphthalide A (Zheng *et al*., 2018b). Both these compounds showed antibacterial activities with the minimum inhibitory concentrations value of 44 µg/mL, 50 µg/mL & 12.5 µg/mL against *E. coli, S. aureus* and *Bacillus subtilis* respectively. The cyclic pentapeptides were isolated and reported from the endophytic *Xylaria* sp. of the chinese medicinal plant *Sophora tonkinensis* (Xu *et al*., 2017). These compounds were commonly known as xylapeptide and exhibited selective antibacterial activities with minimum inhibitory concentrations of 12.5 µg/mL against *Bacillus* sp. also showed moderate antibacterial activity against various bacteria including the pathogenic *S. aureus* (MIC 6.25-12.5 µg/mL). Furthermore, xylapeptide B showed moderate antifungal activity against *Candida albicans* with a MIC of 12.5µg/mL. The antifungal agent griseofulvin (Fig. 4) which was originally found in *P. griseofulvum* is well studied and even clinically applied against dermatophytosis. However, in order to research for more potent derivatives is ongoing using the novel *X. cubensis* as an alternative producer for the same antifungal agent. Hence, the research group of Paguigan *et al*., (2017) reported and isolated semisynthetically the griseofulvin derivatives of 7-fluoro-7-dechlorogriseofulvin showed an activity similar to griseofulvin against the skin infection causing *Microsporum gypseum*.



(Kevin Becker & Marc Stadler 2021)

Fig 4: Recently reported bioactive Compounds obtained from the species of *Xylaria*

The broad spectrum of infections due to multidrug-resistant *S. aureus* (MRSA) varies from mild skin infections to serious and invasive diseases such as septicaemia, pneumonia, endocarditic, deep-seated abscesses including food poisoning, and toxic shock syndrome (Tenover *et al*., 2000; Holmes *et al*., 2005). Over the past few years, a notable increase in antibiotic resistance among Gram-negative bacteria recovered from hospitalized patients has been reported, especially for critically ill patients (Fridkin *et al*., 2001). Infections caused by multidrug-resistant Gram-negative bacteria, especially multidrug-resistant *P. aeruginosa* (MRPA), have been associated with increased morbidity, mortality, and costs. *P. aeruginosa* strains are frequently resistant to multiple antimicrobial agents, and the morbidity and mortality of infections (Niederman 2001, Paladino *et al*., 2002). In this regard, Ramesh *et al*., (2016, 2015a; 2015b, and 2012a; 2012b) studied and reported significant antibacterial activity of both natural fruiting bodies and cultural filtrate crude extract as well as partial purified fraction against multidrug resistant bacterial pathogens of *S. aureus* and *P. aeruginosa*.

Likewise, Surup *et al*., (2014) sporotrichosis of xylarialean fungus shows very strong antifungal effects against fungal pathogens. Ezra G Baraban *et al*., (2013) studied and reported that an antifungal agent xyolide which was isolated from an Amazonian endophytic fungus *X. feejeensis* (Table 4). They tested its bioactive nonenolide called xyolide and it has exhibited an antifungal activity with the MIC value of 425 μM against *Pythium ultimum*. Hacioglu *et al*., (2011) reported that the ethanol extract of fruiting bodies in *X. polymorpha* inhibited the growth of *E. coli, S. aureus, P. aeruginosa* and *Candida albicans*.

Wu *et al*., (2011) reported the isolation and structural elucidation of antifungal proline containing cyclopentapeptides from an endolichenic *Xylaria* sp. They were isolated 10 bioactive compounds such as two new cyclic pentapeptides and the known blazein, ganodesterone, ergosterin, cerevisterol, 24-methylcholesta-4,6,8, 22-tetraen-3-one, 5,8-epidioxyergosta-6,22-dien-3-ol, 16-R-D-mannopyranosyloxyisopimar-7-en-19-oic acid and 16-hydroxy isopimar-7-en-19-oic acid. Further, all the compounds were evaluated for synergistic activity with ketoconazole against fungal pathogens. Among them, cyclic pentapeptide exhibited an effective synergistic antifungal activity with 0.004 µg/mL ketoconazole against *C. albicans*. Gloger's group found that extracts from cultures of *Xylaria* sp. showed moderate antifungal and antiinsecticidal activity. Subsequent chemical studies of this extract led to the isolation of four triterpenoid glycosides named as kolokosides A to D. The kolokosides appear to be members of the fernane class of triterpenoids. Among these compounds, kolokosides A exhibited antibacterial activity against gram positive bacteria (Deyrup *et al*., 2007). Jang *et al*., (2007) isolated xylarinic acids A and B from the fruiting bodies *X. polymorpha*. These novel compounds had antifungal activity against plant pathogenic fungi. Park *et al*., (2005) reported that novel dechlorogriseofulvin and griseofulvin metabolites of the *Xylaria* sp. F0010 displayed potent antifungal activity against plant pathogenic fungi with lower IC50 value of 30 µg/ml. Similarly, Healy *et al*., (2004) reported that the xanthones isolated from *Xylaria* had an effective antibacterial activity against *E. coli*, *Streptococcus pneumoniae*, *Enterococcus faecalis*, *P. aeruginosa* and *S. aureus*.

Future prospective of *Xylaria*

A vast study reported and envisioned that *Xylaria* as an endophytic as well as macro fungus forms a store house of diverse biologically active natural products. Whereas the number of compounds extracted and purified from the species of *Xylaria* entering in the field and clinical trials is said to be limited. Some of the future requirements for avenues in research and development are certainly optimization of growth condition at standard laboratory set up is a crucial stage in isolation of bioactive compounds from *Xylaria* research, widest possible screening for bioactive compounds, extraction of bioactive compounds with the organic solvents, purification of crude extract by chromatographic methods, in-vitro as well as in-vivo pharmacological screening of purified fraction and finally development of commercial bioactive products.

Conclusion

The chemical diversity bearing pharmaceutical potential thus implied reaches beyond the plant kingdom. Most of these compounds exhibit excellent pharmacological activities and are helpful for the invention and discovery of bioactive compounds in future. Moreover, *Xylaria* actually comprises several thousands of species of which the majority remains to be recognized and also to be an untapped and formally described for its bioactive natural products and its will be presumed to push forward to the frontiers of drug discovery.

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Chapter - 4
Examples of Plant-Derived Drugs

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Chapter - 4

Examples of Plant-Derived Drugs

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Abstract

Plant obtained compounds that have recently undergone development include the anticancer agents, taxol and camptothecin, the Chinese, antimalarial, artemisinin drug and the Ayurvedic drug forskolin. These and lots of other examples serve for instance the sustained value of plant-derived secondary metabolites as useful compounds for drug development. Plant derived natural products have long been and can still be extremely important as sources of medicinal agents and models for the synthesis and semi-synthesis of novel substances for treating many diseases. Many of the medicinally important plant derived pharmaceuticals are essential in introducing the age of modern medicine and therapeutics and a few of this substance. Medicinal plants became the most objects of chemists, biochemists, and pharmaceutics. Their investigation plays a crucial role in discovering and developing new drugs that probably have more efficacy and no side actions like the latest drugs.

Keywords: ayurvedic, medicinal plants, natural products, drugs

Introduction

Medicinal plants have historically proven their significance as a source of molecules with healing potential and present days so far describe a crucial tool for the recognition of novel drug leads. India is one of the countries where various traditional systems of medicines are used. Ayurveda, Siddha, Unani, Homeopathy and Tibetan system of medicines are essential ones. These systems have a stimulating task in bioprospecting new medicines. Many modern drugs have their origin in traditional medicines. An outsized part of the Indian population even today depends on the Ayurvedic system of medicine. ‘An ancient science of life’ the documented treaties in Ayurveda are Charaka and Sushruta Samhita.

Medicinal plants are in use for untold centuries and have provided authentic and effective sources in treating and preventing diseases.

Medicinal plants are a vital tool of usual and uncostly new drugs for people ubiquitously in the planet. There is a need for suitable recognition of drugs and collecting them at accurate times and grading them for attributes.

The great need of collecting good herbarium material for taxonomic identification of the collected species must be stressed. The base of the pharmacognostic profile of the plants will help in standardization which can help within the identification of plants. There is a requirement for the protection of all usable plant species and also its cultivation, preservation and evaluation of germplasm for use in future. Primarily among the foremost vulnerable plant species in India, the predominant over-exploited are the medicinal plants. The East Indian snakeroot *Rauvolfia serpentina* (L.) Benth. ex Kurz has been used for hundred years as a native East Indian medicinal plant, and its main active principle reserpine is now utilized in western medicine as an antihypertensive and tranquilizer. Accordingly, other bioactive and poisonous plants with vast folklore histories have yielded cardiac (Digitalis) glycosides.

Natural products as drug: a historical perspective

The first written records on medicinal plants date back to about 2600 BC and report the presence of the medicinal system in Mesopotamia, which includes about 1000 plant-derived medicines. Traditional Chinese medicine has been broadly documented over thousands of years (Unschuld, 1986) and therefore the documentation of the Indian Ayurveda system dates back to the first millennium BC (Patwardhan, 2005).

Collection of drugs

The time of the collection of vegetable drugs is of prime need and until we may not be able to make extensive generalizations, still the following general rules for the collection of various drugs may be given:

1) Roots, rhizomes and barks should be collected immediately before the vegetative life-processes begin (in the spring) or immediately after the vegetative processes cease (usually in the fall).
2) Leaves should be collected when the $C0_2$ assimilation process is most active; usually about the time of development of the flowers and before mature development of fruit and seed.
3) Flowers should be collected before or just about the time of pollination.
4) Fruits should be collected near the ripening period (i.e., full-grown but unripe).
5) Seeds should be collected when fully matured.

The valuation of drugs

In the identification of medicinal drugs few traits are taken under consideration, like color, aroma general appearance, structure, texture, etc., these at the equivalent time depicting during a greater or less degree the qualitative value of the drug. While these characteristics may enable the expert to explore very slight variations in quality and to calculate approximately the value of a given drug, still the true value is based upon the quantity of the medicinal principles or so-called active constituents. The methods employed within the valuation of drugs may be grouped as follows:

1) **Chemical methods:** They are more generally applied and generally involve the isolation and estimation of the active principles.
2) **Physical methods:** It involves such processes as the determination of specific gravity of the drug as of jalap or the assessment of the elasticity or measurement of the fibers as of cotton and still other special methods applied to individual drugs giving indirectly their valuation.
3) **Microscopical methods:** It valuated may oftentimes be used when other methods fail as, for ex: when foreign starches are added to starchy products within the cereals and spices. Microchemical reaction can also be depended upon in some instances to point the value of a drug as in *Strophanthus* where the value of the drug depends directly upon the number of seeds giving a green coloration with sulphuric acid.
4) **Biological methods:** It includes the importance of the effects of drugs upon animals or plants.
5) **Ethnopharmacological methods:** It includes the selection of the test samples based on traditional medicinal usage of the plant species.
6) **Ecological methods:** It involves the choice of samples that supported the interactions between organisms and their natural world on the entire that plant secondary metabolites affect ecological functions from which a probable medicinal uses for humans are often derived.

Table 1: Some Examples of Economically Important Plant-Derived Drugs (Lewis *et al*., 1977; Tyler *et al*., 1988; Farnsworth, 1973, 1966)

S. N.	Plant sources	Drugs/Alkaloid	Family	Product	Activity
1.	*Acacia senegal*	Arabin	Combretaceae	Evecare	Dental problem
2.	*Achyranthes aspera*	Ecdysterone, Saponins C, D	Amaranthaceae	Cystone tablet	Astringent, diuretic
3.	*Adonis vernalis*	a) Adonis b) Adonidine	Ranunculaceae	Adonis vernalis	Anti-asthmatic, cardiac disorder
4.	*Ammi visnaga*	a) Visnaga b) Khellin	Umbelliferae	Lukoskin oral drops	Muscle relaxant Anti-asthmatic
5.	*Artemisia annua*	Artemisinin	Asteraceae	Artekin	Anti-malaria
6.	*Andrographis paniculata*	Andrographolide	Acanthaceae	Sage liverex	Baccillary dysentery
7.	*Berberis vulgaris*	Berberine	Berberidaceae	Berberis	Antidysentric
8.	*Betula alba*	Betulinic acid	Betulaceae	Birch oil	Anticancerous
9.	*Cassia acutifolia*	Sennoside A, Sennoside B	Leguminosae	Constivac, Isova powder, Kultab tablet	Laxative, carminatives
10.	*Catharanthus roseus*	a) Vincristine b) Ajmalthine c) Serpentine d) Vinblastine e) Ajmalicine	Apocynaceae	Cytocristin	Antileukaemic Antiarrhythmic Tranquilizer Antitumor
11.	*Cephaelis ipecacuanha*	a) Emetine b) Pscychotrines	Rubiaceae	Ipecac syrup	Amoebicide, emetic, Anti-HIV
12.	*Chondodendron tomentosum*	Curare	Menispermaceae	Tubocurarine	Skeletal muscle relaxant
13.	*Chrysanthemum cinerariaefolium*	Pyrethrin	Compositae	Pyrethrin	Insecticide
14.	*Dioscorea deltoidea*	Diosgenin	Dioscoreaceae	Lanoxin tablets	Antifertility
15.	*Digitalis lanata*	a) Digoxin b) Lanatoside A, B, C c) Acetyligitoxin	Scrophulariaceae	Acetyldigoxin	Cardiotonic
16.	*Duboisia myoporoides*	a) Atropine b) Hyoscyamine c) Scopolamine	Solanaceae	Duboisia 30C	Stomach disorders, pre-surgical muscle relaxant
17.	*Galanthus caucasicus*	Razadyne, Galantamine	Amaryllidaceae	Galantamine hydrobromide extended release capsules	Dementia associated with Alzheimer's disease
18.	*Helianthus tuberosus*	Inulin as fructosan	Compositae	Gomine helianthus tuberosus powder	Antidiabetic, antirheumatism
19.	*Ocimum sanctum*	Eugenol, citral,	Labiatae	Nomarks,	Antidiabetic,

		epigenin		Sualin	antipyretic
20.	*Rauvolfia serpentina*	Reserpine	Apocynaceae	Rauwolfia serpentine tablets	Antihypertensive, psychotropic, tranquilizer
21.	*Pilocarpus jaborandi*	Pilocarpine	Rutaceae	Jaborandi	Cholinergic, dilate pupils
22.	*Erythroxylum coca*	Cocaine	Erythroxylaceae	Fluid extract coca	Local anesthetic

Table 2: Drugs derived from Allopathy

S.N.	Plant Name	Drug/Alkaloid	Family	Product	Activity
1.	*Camptotheca acuminata*	Camptothecin	Nyssaceae	Irinotecan	Ovarian, lung cancer, antitumor
2.	*Citrus limon*	Lemon peel, Luteolin (Flavone), Naringin (Flavanone)	Rutaceae	Ultra doux conditioner	Carminative, stimulant, vit C source
3.	*Coleus forskohlii*	Forskolin	Lamiaceae	Forskolin forte	Anti-glaucoma
4.	*Cinchona calisaya*	Quidine, quinine, cinchonine, cinchonidine	Rubiaceae	Quinalaquin	Antimalarial, antidiarrhoeal
5.	*C. ledgeriana*	a) Quinidine b) Cinchonidine	Rutaceae	Herbipyrin tablet, M.P. 6 Capsules	Cardiac depressant, Rheumatism, anti-malarial
6.	*Papaver somniferum*	Morphine, Codeine	Papaveraceae	Oxycontin	Cough suppressant, anti-cancer
7.	*Psoralea corylifolia*	Psoralea	Leguminosae	Purim, Arena, Purodil	Aphrodisiac
8.	*Santalum album,*	Sandal	Santalaceae	Abana, Lukol	Diuretic, cardiotonic,
9.	*Smilax ornata*	Sarsaparilla	Liliaceae	Purodil capsules	Chronic skin diseases
10.	*Salix alba*	Salicin	Salicaceae	Aspirin	Analgesic, Antipyretic
11.	*Tricosanthes kirilowi*	Tricosanthin	Cucurbitaceae	Tricosanthes kirilowi dried fruit liquid extract	Anti-cancer, anti-inflammation, anti-bronchial

Table 3: Drugs derived from Homeopathy

S.N.	Plant Name	Drug/Alkaloid	Family	Product	Activity
1.	*Abrus precatorius*	Abrol, abasine	Fabaceae	Jequirity	Treatment of eyes
2.	*Ailanthus glandulosa*	Ailanthone	Simaroubaceae	Ailanthus	Anthelmintic

3.	*Anemone pulsatilla*	Anemonin	Ranunculaceae	Pulsatila	Anti-rheumatism, gastric disorders
4.	*Bryonia dioica*	Cucurbitacin glucosides	Cucurbitaceae	Bryonia	Bronchitis, dry cough
5.	*Calendula officinalis*	Coumarins	Asteraceae	Calendula	Wounds, burn, soothes skin
6.	*Chenopodium anthelminticum*	Ascaridole	Amaranthaceae	Chenopodium	Roundworm, tapeworm infection
7.	*Cimicifuga racemosa*	Cimicifugic acid, Fucinolic acid	Ranunculaceae	Cimicifuga	Amenorrhoea, Neuralgic
8.	*Conium maculatum*	N-methylconiine, conhydrine	Apiaceae	Conium	Paralysis, cancer
9.	*Eugenia jambolana*	Myricetin	Myrtaceae	Jambul	Anti-diabetic
10.	*Quercus alba*	Quercitannic acid	Fagaceae	Quercus	Bed sores, astringent
11.	*Thymus vulgaris*	Carvacrol, thymol	Labiatae	Thymol	Ringworm, antiparasitic

Table 4: Drugs derived from Ayurvedic

S.N.	Plant Name	Drug	Family	Product	Medicinal use
1.	*Aegle marmelos*	Bael	Rutaceae	Chyawanprash, Bilwadi churna	Diarrhoea, Dysentry
2.	*Adhatoda vasica*	Vasaka vasicinol, vasicinone, adhatonine	Acanthaceae	Vasavaleha, vasaka capsule	Respiratory disorders
3.	*Areca catechu*	Arecoline	Palmaceae	Himplasia, khadiradi bati	Anthelmintic, aphrodisiac
4.	*Asparagus racemosus*	Shatavari	Liliaceae	Satavari kalp, Diabecon	Aphrodisiac, laxative
5.	*Centella asiatica*	Brahmoside, brahminoside, asiaticoside	Umbelliferae	Geriforte, Menosan, Mentat	Tonic, improve memory, immunomodulator
6.	*Cinnamomum zeylanicum*	Cinnamon	Lauraceae	Chyawanprash, Sutsekhar ras	Carminative
7.	*C. camphora*	Camphene	Lauraceae	Dabur balm	Antipruritic
8.	*Citrus vulgaris*	Bitter orange peel	Rutaceae	Dabur vatica body shampoo	Stomachic
9.	*Cymbopogon flexuosus*	a) Lemongrass b) Lonones	Poaceae	Sage lion balm	Mosquito repellant
10.	*Datura metel*	a) Hyoscine b) Scopolamine.	Solanaceae	Jatifaladi Bati, Jatyadi tail	Anticholinergic
11.	*Datura stramonium*	Scopolamine	Solanaceae	Maharasayan vati	Antispasmodic

12.	*Eclipta alba*	Ecliptal	Asteraceae	Eclipta	Skin and hair disorders
13.	*Hyoscyamus niger*	Hyoscyamine	Solanaceae	Sarpagandhaghan vati, Brahmi vati	Anticholinergic
14.	*Mentha piperita*	Peppermint	Labiatae	Dabur lal tooth powder	Stimulant, Nausea
15.	*M. spicata*	Pudina	Labiatae	Rheumatic gel	Carminative
16.	*Picrorhiza kurroa*	Katurohini	Plantaginaceae	Purim, Aptikid	Hepatoprotective
17.	*Plantago ovata*	Ispaghula	Plumbaginaceae	Isabgol, Trifgol	Laxative, anti-diarrhoeal
18.	*Semecarpus anacardium*	bhilawanol	Anacardiaceae	Sanjivani vati, Patrangasava	Leprous affections, nervous debility
19.	*Swertia chirayta*	Chirayita	Gentianaceae	Safi, Mehmudgar bati	Appetite stimulant, ophthalmic appetizer
20.	*Tinospora cordifolia*	Guduchi, tinocordifolisoide	Menispermaceae	Guduchi tablet, Abana	Rejuvenator, antioxidant

Table A: Drugs derived from Flowering plant part (Seeds)

S.N.	Plant Name	Drug/Alkaloid	Family	Product	Activity
1.	*Delphinium staphisagria*	Staphisagria	Ranunculaceae	Delphinium staphisagria remedia globuli	Toothache, genitor-urinary
2.	*Elettaria cardamomum*	Cineole	Zingiberaceae	Koflet	Stomachic
3.	*Garcinia indica*	Kokum	Guttiferae	Bioslim	Cosmetic
4.	*Gossypium harbaceum*	Linoleic	Malvaceae	J.P. Message oil	Emollient
5.	*Linum usitassimum*	Linseed oil, Linamarin	Linaceae	Canisep and Scavon	Gonorrhoea
6.	*Myristica fragrans*	Nutmeg	Myristicaceae	Kumaryasava	Flatulence
7.	*Nigella sativa*	Nigellimin, nigellidin, nigellicin.	Ranunculaceae	Anti-dandruff shampoo	Antiinflammatory, antihypertensive, antidiarrhoeal
8.	*Prunus amygdalus*	Almond oil	Rosaceae	Badam roghan oil	Emollient
9.	*Ricinus communis*	Ricinoleic acid	Euphorbiaceae	Lip balm, muscle joint rub	Laxative, antitumorous
10.	*Strophanthus kombe*	Strophanthus	Apocynaceae		Chronic heartproblems
11.	*Strychnos nux vomica*	Nuxvomica, Strychnine, Brucine	Loganiaceae	Neo tablet	Laxative, Nervous disorder, paralysis
12.	*Trachyspermum ammi*	Aptikid	Apiaceae	Aptikid	Antispasmodic

Table 5: Drugs derived from Plant part (Roots and rhizomes)

S.N.	Plant Name	Drug/Alkaloid	Family	Product	Activity
1.	*Aconitum napellus*	a) Aconite b) Aconitine	Ranunculaceae	J.P. Painkill oil	Rheumatism, neuralgia
2.	*Acorus calamus*	Acorus	Arecaceae	Mahamarichadi tel	Expectorant
3.	*Atropa belladonna*	a) Belladonna b) Atropine	Solanaceae	Belladonna plaster	Anticholinergic
4.	*Brassica nigra*	Mustard oil, Allyl isothiocyanate	Brassicaceae	Dabur mustard oil	Rubefacient
5.	*Carthamus tinctorius*	Safflower oil, oleomargarine	Compositae	Saaf organic eraser body Oil	Edible, artherosclerosis
6.	*Colchicum luteum*	Colchicum	Liliaceae	Aujai capsules	Gout
7.	*Curcuma longa*	Curcumin I, II, III, Curcuminoids, Tetrahydrocurcuminoides	Zingiberaceae	Respinova, J.P. Nikhar oil, Diabecon, Purian	Antinflammatory, anticancer, Antioxidants, antiinflammatory
8.	*Glycyrrhiza glabra*	Glycyrrhiza, Licorice	Leguminosae	Herebolex, Yasti madhu	Bronchitis, skin whitening
9.	*Nardostachys jatamansi*	Nardostachone	Valerianaceae	Dashmularishta	Antirrhythmic
10.	*Podophyllum peltatum*	a) Podophyllum b) Etoposide	Berberidaceae	Podowart, Podophyllotoxin	Antiviral, Anticancer
11.	*Polygala senega*	Senega	Polygalaceae	Senega snakeroot	Expectorant
12.	*Rauwolfia serpentina*	Rauwolfia, ajmalicine	Apocynaceae	Confido, Lukol, Serpina,Sarpagandhan bati	Antihypertensive, blood pressure
13.	*Sesamum indicum*	Sesame oil, oleic, linoleic acid	Pedaliaceae	Dabur lal tel	Antioxidant, insecticidal
14.	*Valeriana wallichi*	Valerian	Valerianacee	Anxocare, Mentat	Blood pressure
15.	*Zingiber officinale*	Gingerol	Zingiberaceae	Hajmola, Strepsils	Antiemetic, antioxidant

Table 6: Drugs derived from Plant part (Stems)

S.N.	Plant Name	Drugs/Alkaloids	Family	Product	Activity
1.	*Liquidambar orientalis*	Storax	Hamamelidaceae	Compound Benzoin Tincture	Antiseptic, parasiticide
2.	*Myroxylon balsamum*	Balsam of Peru	Papilionaceae	Aubrey Organics Natural sun SPF 12 Vitamin C	Miticide
3.	*Rosmarinus officinalis*	Cornosolic acid	Lamiaceae	Anti-dandruff shampoo	Gastric debility
4.	*Styrax tonkinensis*	Ciniferyl benjoate	Styraceae	Friar's Balsam	Antioxidative
5.	*Styrax benzoin*	Sumatra benzoin	Styraceae	Friar's Balsam	Diuretic

Table 7: Drugs derived from Plant part (Pith, wood and bark)

S.N.	Plant Name	Drugs/Alkaloids	Family	Product	Activity
1.	*Acacia catechu*	Phlobatannin catechutannic acid	Leguminosae	Koflet lozenge	Astringent
2.	*Cassia aromaticum*	Cassia bark	Lauraceae	Madhudoshantak	Gastric debility
3.	*Cinchona officinalis*	Quinine	Rubiaceae	Cinchona officinalis 30C	Treatment of malaria.
4.	*Commiphora mukul*	Guggul	Burseraceae	Arogyavardhini gutika	Lowers LDL and VLDL
5.	*Holarrhena antidysenterica*	Kurchi	Apocynaceae	Mahamanjishthadi kwath, Purodil capsules	Antidysentric
6.	*Pterocarpus marsupium*	Kinotannic acid	Leguminosae	Diabecon	Astringent
7.	*Saraca indica*	Ashoka, Anthocyanin	Leguminosae	Ashokarisht	Uterine tonic
8.	*Symplocos racemosa*	Lodh	Symplocaceae	Evecare, Styplon	Red, yellow dye
9.	*Terminalia arjuna*	Arjunic acid	Combretaceae	Geriforte, Liv 52, Arjun churna	Angina, hypertensive

Table 8: Drugs derived from Plant part (Flowers)

S.N.	Plant Nmae	Drugs/Alkaloids	Family	Product	Activity
1.	*Arnica montana*	Arnicin	Compositae	Arnica montana 30X	Anti-inflammation
2.	*Calendula officinalis*	Calendulin	Compositae	Calendula officinalis ointment	Antimicrobial, antioxidant

3.	*Cannabis sativa*	a) Cannabidiol b) Cannabidolic acid	Cannabinaceae	Bilwadi churna	Muscle relaxant, hallucinogenic
4.	*Capsicum annum*	a) Capsicin b) Casanthin	Solanaceae	Capsigyl-D	Postherpetic neuralgia
5.	*Citrullus colocynthis*	Colocynth	Cucurbitaceae	The body pure	Gastralgia, diarrhea

Table 9: Drugs derived from Plant part (Fruits)

S.N.	Plant Name	Drug/Alkaloids	Family	Product	Activity
1.	*Anethum graveolens*	Dill, D-limonene	Umbelliferae	Woodward's gripe water	Flatulence
2.	*Carica papaya*	β-Cryptoxanthin	Caricaceae	Papain	Reduce incidence of blood clots
3.	*Carum carvi*	Caraway, Carvene	Umbelliferae	Gripe water	Dyspepsia
4.	*Carum carvi*	Umbelliferone	Umbelliferae	Bilwadi churna	Rheumatism
5.	*Cuminum cyminum*	Cumin aldehyde	Umbelliferae	Hajmola	Carminative
6.	*Embelia ribes*	Viranga, vilangin	Myrisinaceae	Diakof, Herbolax, Koflet	Anthelmintic, contraceptive
7.	*Emblica officinalis*	Phyllantidine, phyllantine	Euphorbiaceae	Triphala churna, Chyawanprash	Improves memory
8.	*Foeniculum vulgare*	Anethole	Umbelliferae	Dabur hajmola, Dabur janum Gunti	Estrogen like activity, lactation
9.	*Olea europoea*	Olive oil, Oleic acid, Luteolin (Flavone)	Oleaceae	Figaro oil	Laxative, demulcent
10.	*Papaver somniferum*	a) Dextromethorphan b) Verapamil c) Codeine d) Noscapine e) Papaverine	Papaveraceae	Morphine, codeine	Analgesic, antitussive Angina Sedative Cough suppressant
11.	*Pimpinella anisum*	Umbelliferone, scopoletin	Umbelliferae	Pimpinella anisum	Antispasmodic, carminative
12.	*Terminalia chebula*	Haritaki, chebulinic acid	Combretaceae	Haritakh churna, Triphala churna, Tentex forte	Antiviral, bleeding gums, Antiasthmatic

13.	*Terminalia bellerica*	Gallic acid	Combretaceae	Triphala churna	Dyspepsia, diarrhoea
14.	*Tribulus terrestris*	Tribulustrine	Zygophyllaceae	Bonnisan, Dhatupoushtik churna	Aphrodisiac

Table 10: Drugs derived from Plant part (Leaves)

S.N.	Plant Name	Drug/Alkaloids	Family	Product	Activity
1.	*Aloe vera*	Aloin, emodin	Liliaceae	Diabecon, kumariasava	Purgative, antiviral
2.	*Bacopa monnieri*	Bacoside	Plantaginaceae	Brahmi	Memory enhancement
3.	*Cassia tora*	Chrysophanol	Caesalpiniaceae	Mahamarichadi Tail	Skin diseases
4.	*Celastrus paniculatus*	Malkangni	Celastraceae	Geriforte, Himcolin	Aphrodisiac, brain tonic
5.	*Eucalyptus globulus*	Eucalyptol	Myrtaceae	Canisep, cold balm	Febrifuge
6.	*Copernicia prunifera*	Carnaubic acid	Palmae	Carnauba wax	Cosmetics, deodorants
7.	*Digitalis purpurea*	a) Digitoxin b) Gitalin	Scrophulariaceae	Lanoxin tablets	Cardiotonic
8.	*Gaultheria procumbens*	Methyl salicylate	Ericaceae	Dabur balm	Diuretic, rubefacient
9.	*Tylophora indica*	Tylophorine, Tylophorinine, Tylophorinidin	Asclepiadaceae	Geriforte Aqua	Antiinflammatory, antidiarrhoeal, antidysentry
10.	*Withania somnifera*	a) Withanolides b) Withaferin A	Solanaceae	Geriforte, Ashvagandha tablet, Balarishta	Anticancer, Parkinson's disorder, Alzheimer's disorder

Table 11: Drugs derived from Plant part (Exudations, juices and other plant products)

S.N.	Plant Name	Drug/Alkaloids	Family	Product	Activity
1.	*Allium sativum*	Allicin, Alliin, Quercetin (Flavonols)	Liliaceae	Lashunadi bati	Carminative, antiinflammatory
2.	*Ananas comosus*	Bromelain	Bromeliaceae	Bromelain	Fabrinolytic
3.	*Cocos nucifera*	Coconut oil	Palmae	Lip balm, Evecare	Dietary
4.	*Crocus sativus*	Saffron	Iridaceae	Tentex forte	Spasmolytic

5.	*Eugenia caryophyllus*	Eugenol	Myrtaceae	Himsagar tail	Local an aesthetic
6.	*Hevea braziliensis*	Caoutchouc	Euphorbiaceae		
7.	*Zea mays*	Corn oil	Gramineae	Esoban ointment	Dermatitis

Table 12: Drugs derived from Pteridophyte

S.N.	Plant Name	Drug/Alkaloids	Family	Product	Activity
1.	*Asplenium scolopendrium*	Gallic acid	Aspleniaceae	Scolopendrium vulgare	Antibacterial, digestive disorders
2.	*Dryopteris filix-mas*	Phloroglucinol Filicic acid	Dryopteraceae	Paratrex, Flix max	Gastric disorders
3.	*Equisetum arvense*	Palustrine	Equisetaceae	Equisetum arvense	Stop bleeding
4.	*E. hyemale*	Kaempferol	Equisetaceae	Equisetum hyemale	Antioxidant
5.	*Lycopodium clavatum*	Apigenin	Lycopodiaceae	Lycopodium	Antidiarrhoeal, stomach ache
6.	*Huperzia serrata*	Huperzine A	Lycopodiaceae	Huperzine A	Alzheimer's
7.	*Selaginella flabellate*	Selaginellins	Selaginellaceae	Selacin	Control fever, menstruation

Table 13: Drugs derived from Gymnosperm

S.N.	Plant Nmae	Drug/Alkaloid	Family	Product	Activity
1.	*Abies balsamea*	Camphor	Pinaceae	Canada balsam	Antidysentric
2.	*Cephalotaxus harringtonia*	a) Synribo b) Cephalotoxine	Cephalotaxaceae	Cephalotaxus	Anti-cancer, Leukemia
3.	*C. circinalis*	Amentoflavone	Cycadaceae	Anodyne	Narcotic
4.	*Chamaecyparis lawsoniana*	Terpinen-4-ol	Cupressaceae	Cupressus lawsoniana	Antioxidant, antiviral
5.	*Ephedra distachya*	Ephedrine	Ephedraceae	Ephedra	
6.	*Ephedra sinica*	a) Ephedrine b) Pseudoephedrine	Ephedraceae	Bronchial asthama, cold	Antihistamine
7.	*Ephedra gerardiana*	a) Ephedra b) Pseudoephedrine c) Norpseudoephedrine	Ephedraceae	Ephedrine sulphate	Antiallergenic Coughsuppressant Vasodilator
8.	*Ferula asafoetida*	Asafoetida	Apiaceae	Madhudoshantak	Antispasmodic
9.	*Ginkgo biloba*	Ginkgolides A, B, C	Ginkgoaceae	Ginkgo	Antiasthmatic, antioxidant, memory enhancer
10.	*Juniperus communis*	Gallocatechin	Cupressaceae	Juniperus communis	Antioxidant, antiinflammatory
11.	*J. virginianan*	Cupressuflavone	Cupressaceae	Juniperus virginiana	Antimicrobial
12.	*J. sabina*	Siderin	Cupressaceae	Savin oil, Sabina	Abortifacient
13.	*Macrozamia spiralis*	Macrozamin	Zamiaceae	Macrozamia	Toxic
14.	*Panax ginseng*	Ginsenosides	Araliaceae	Ginseng	Anticancer
15.	*Picea mariana*	α-terpineol	Pinaceae	Abies nigra	Antiseptic
16.	*Pinus lambertiana*	Lambertianic acid	Pinaceae	Pinus lambertiana	Laxative
17.	*Pinus longifolia*	Turpentine	Pinaceae	Oleoresin,	Rubefacient

				Rumalaya gel	
18.	*P. pinaster*	Procyanidins	Pinaceae	Pycnogenol	Antioxidant
19.	*P. sylvestris*	Terpinolene	Pinaceae	Pinus sylvestris	Expectorant
20.	*Pseudotsuga manzeisii*	Bornyl acetate	Pinaceae	Pseudotsuga manzeisii	Antiseptic, sore throat
21.	*Sequoia sempervirens*	Sequoitol, pinitol, myoinositol	Taxodiaceae	Sequoia & blue lily antiwrinkle	Anti-ageing, antiwrinkle
22.	*Taxus baccata*	Taxanes	Taxodiaceae	Taxus baccata	Anticancer
23.	*Taxus brevifolia*	Taxol (Paclitaxel)	Taxaceae	Taxus brevifolia	Anticancer
24.	*Thuja occidentalis*	Thujone	Cupressaceae	Thuja occidentalis	Anti-inflammatory, Anti-HIV
25.	*T. plicata*	α-thujone, β-thujone	Cupressaceae	Thuja lobbi	Bronchodilator
26.	*Tsuga canadensis*	α pinene, myrcene	Pinaceae	Abies canadensis	Digestive disorder

Table 14: Drugs derived from Fungi

S.N.	Fungi Name	Drugs/Alkaloids	Class	Product	Activity
1.	*Acremonium chrysogenum*	β-lactam	Ascomycetes	Cephalosporin	Bactericidal
2.	*Amanita pantherina*	Muscimol	Agariomycetes	Muscarine	Analgesic
3.	*Aspergillus fumigatus*	Spirotryprostatin B	Ascomycetes	Fumagillin, gliotoxin	Anticancer
4.	*A. flavus*	Kojic acid	Ascomycetes	Aflatoxin B1, B2, M1	Pesticides
5.	*A. fumigatus*	Fumagillin	Ascomycetes	Antibiotic fumagillin	Antifungal
6.	*A. gallomyces*	Galactomannan	Ascomycetes	Gallic acid	Antioxidant
7.	*Ashbya gossypii*	Ergosterol	Ascomycetes	Riboflavin (vit B_2)	Antiallergic
8.	*A. oryzae*	Asperfuran	Ascomycetes	Kojic acid	Anti-allergic
9.	*A. niger*	Bicoumanigrin, Aspernigrin B	Ascomycetes	Citric acid, gluconic acid, oxalic acid	Disinfectant, Neuroprotective
10.	*A. terreus*	Mevinolin	Ascomycetes	Lovastatin, Gliotoxin	Antifungal
11.	*Candida utilis*	Cholesterol	Ascomycetes	Torula yeast, vit D	Proteolytic
12.	*Cephalosporium*	β-lactam	Ascomycetes	Cephalosporin	Antibacterial
13.	*Claviceps purpurea*	a) Ergometrine b) Bromocryptine c) Ergotamine	Ascomycetes	Lysergic acid (LSD), Ergosterol	Uterus contraction, Parkinson's disease
14.	*Cordyceps sinensis*	Sterol	Ascomycetes	Cordyceps	Anti-ageing
15.	*Clitocybe nebularis*	Nebularine	Basidiomycetes	Muscarine	Antiglaucoma
16.	*Cordyceps sinclairii*	Myriocin	Ascomycetes	Gilenya	Immunosuppressant
17.	*Fusidium coccineum*	β-glucogallin	Sordariomycetes	Fusidic acid	Bacteriostatic
18.	*Fusarium lini*	Lactones	Deuteromycetes	Digitoxigenin, digoxigenin	Cardiac disorder
19.	*Ganoderma lucidum*	Ganoderic acid β	Basidiomycetes	Ganoderma	Anti-HIV
20.	*Gibberella fujikuroi*	Gibberellic acid	Ascomycetes	Gibberellins	Phyto hormone
21.	*Mycelia sterilia*	Glyscavins A, B, C	Deuteromycetes	Myriocin	Immunisuppresant
22.	*Penicillium brevicompatcum*	Mycophenolic acid	Ascomycetes	Compactin	Immunosuppressive
23.	*Penicillium citrinum*	Lovastatin	Ascomycetes	Citrinin, Compactin	Cholesterol lowering

24.	*P. expansum*	Patulin	Ascomycetes	Patulin	Antibiotic
25.	*P. griseofulvin*	Penifulvin A	Ascomycetes	Griseofulvin	Antifungal
26.	*P. islandicum*	Islanditoxin	Ascomycetes	Emodin	Antiinflammatory
27.	*P. notatum*	6-aminopenicillanic acid	Ascomycetes	Penicillin, griseofulvin, mycophenolic acid	Immunosuppressant
28.	*P. stoloniferum*	Mycophenolic acid	Ascomycetes	Mycophenolic acid	Antibacterial
29.	*Pencillium viridicatum*	Ochratoxin A, B, C	Ascomycetes	Ochratoxin	Nephrotoxin, carcinogenic
30.	*Pleurotus ostreatus*	β-glucan	Basidiomycetes	Lovastatin	Cholestrol lowering
31.	*Psilocybe mexicana*	Psilosin	Basidiomycetes	Psilocybin	Hallucinogenic
32.	*Rhizopus stolonifer*	d-lactic acid	Phycomycetes	Fumaric acid, Lactic acid, cortisone	Food acidulant
33.	*Saccharomyces cerevisae*	Farnesene, zymase, Artemisinic acid, Paclitaxel	Ascomycetes	Lactic acid, succinic acid, vit D, Invertase	Antibacterial
34.	*Tolypocladium inflatum*	Tolypocladin	Sordariomycetes	Cyclosporin A	Immunosuppressant
35.	*Yarrowia lipolytica*	α-ketoglutarate	Ascomycetes	Isocitric acid	Anticoagulant

Table 15: Drugs derived from Algae

S.N.	Name of Algae	Drug/Alkaloid	Family	Product	Activity
1.	*Chlorella vulgaris*	Uronic acid	Chlorophyta	Chlorellin	Antibacterial
2.	*Chondria armata*	Domoic acid	Rhodophyceae	Domoic acid	Anthelmintic, antiparasitic
3.	*Chondrus crispus*	Kappa-carrageenin, lambda-carrageenin	Rhodophyceae	Carrageenan, Agar	Antiinflammatory
4.	*Chondria oppositicladia*	Chondriol	Rhodophyceae	Cycloeudesmol	Antibiotics
5.	*Dictyopteris zonoroid*	Zonorol, isozonorol	Phaeophyceae	Zonarol	Antifungal
6.	*Digenia simplex*	α-Kainic acid	Rhodophyceae	α-Kainic acid	Anthelmintic
7.	*Fucus vesiculosus*	kelp	Phaeophyceae	Iodine	Anticoagulant
8.	*Gracilaria lichenoides*	Prostaglandins	Rhodophyceae	Agar	Laxative

9.	*Gambierdiscus toxicus*	Ciguatoxin, Maitotoxin	Dinophyceae	Ciguatoxin CTX	Fish poisoning
10.	*Gonyaulax catenella*	Saxitoxin 1	Dinophyceae	Saxitoxin	Neurotoxin
11.	*Iridaea laminarioides*	Galactan	Rhodophyceae	Galactan sulphuric acid	Anticoagulant
12.	*Laminaria digitala*	Fucoidan, Laminine, kelp	Phaeophyceae	Alginic acid, mannitol, iodine	Dilate cervix, HIV, Herpes simplex viruses.
13.	*Laurencia johnstonii*	Prepacifenol	Rhodophyceae	Laurencia	Antibacterial
14.	*L. filiformis*	Chondriol	Rhodophyceae	Chondriol	Antibacterial
15.	*Lyngbya majuscule*	Curacin A, Dolastatin	Cyanophyceae	Lyngbyatoxin A	Contact dermatitis, Antiproliferative
16.	*Spirulina platensis*	vit A, vit E	Cyanophyceae	Spirulina	Immunostimulant

Table 16: Drugs derived from Bryophytes and Lichens

S.N.	Plant Name	Drug/Alkaloid	Family	Product	Activity
1.	*Cetraria islandica*	Lichenan	Parmeliaceae	lichenin and isolichenin	nauseous medicines
2.	*Cladonia substellata*	Usnic acid	Cladoniaceae	Usnic acid	Antibiotic
3.	*Marchantia polymorpha*	Plagiochin E, marchantins A, B	Marchantiaceae	Lunularic acid	Pulmonary tuberculosis
4.	*Polytrichum commune*	Luteolin	Polytrichaceae	Polytrichum	Antitumor, dissolve stones of kidney, gall bladder
5.	*P. juniperinum*	Communins A(1), B(2)	Polytrichaceae	Polytrichum	Anticancer
6.	*Sphagnum strictum*	Sphagnum acid	Polytrichaceae	Sphagnol	Antiseptic, anticandidal

Table 17: Drugs derived from Bacteria

S.N.	Plant Nmae	Drug/Alkaloid	Family	Product	Activity
1.	*Bacillus polymyxa*	Bacillomycin D, L	Paenibacillaceae	Polymyxin B, Collistin	Bactericidal
2.	*B. subtilis*	Fengycin	Paenibacillaceae	Bacitracin, Amicoumacin	Antibiotics
3.	*Lactobacillus acidophillus*	Lactic acid	Lactobacillaceae	Probiotics	Vaginal infections
4.	*Escherichia coli*	Shiga toxin	Enterobacteriaceae	Clindamicin, Ciprofloxacin, Vancomycin	Antibacterial, Antibiotic, Intestinal inflammation
5.	*Micromonospora purpurea*	Gentamicin C1	Micromonosporaceae	Gentamicin	Meningitis
6.	*Pseudomonas aeruginosa*	Phenazines	Pseudomonadaceae	Tobramycin, Vancomycin	Antibacterial, Intestinal inflammation
7.	*Streptomyces* spp.	Actinomycin D	Streptomycetaceae	Actinomycin D	Sarcoma and gall tumors
8.	*Streptomyces avermitilis*	Ivermectin B1a, B1b	Streptomycetaceae	Avermectin	Antinematodal
9.	*Streptomyces aureofaciens*	Tetracycline	Streptomycetaceae	Aureomycin	Antibacterial
10.	*S. caespitosus*	Mitomycins A, B, C	Streptomycetaceae	Mitomycin C	Gastric, colorectal cancer
11.	*S. carbophilus*	Pravastatin	Streptomycetaceae	Compactin	Hypocholesterolemic
12.	*S. capreolus*	Capreomycin sulphate	Streptomycetaceae	Capreomycin	Antituberculosis
13.	*S. coeruleorubidus*	Daunomycin	Streptomycetaceae	Daunomycin	Antileukemic
14.	*Streptomyces clavuligerus*	Clavulanic acid	Streptomycetaceae	Clavulanic acid	Antimicrobial, respiratory tract infections
15.	*S. erythreus*	Erythromycin A	Streptomycetaceae	Erythromycin	Pneumonia, whooping cough
16.	*S. fradiae*	Tylosin, Fosfomycin D	Streptomycetaceae	Neomycin	Wounds, ulcers, burn
17.	*S. griseus*	Streptomycin	Streptomycetaceae	Streptomycin, actidine	Pulmonary tuberculosis, plague, Antimicrobial

18.	*S. lincolinensis*	Lincomycin	Streptomycetaceae	Clindmycin	Antibacterial
19.	*S. mediterranei*	Rifampin	Streptomycetaceae	Rifampicin	Oral contraceptives
20.	*S, nodosus*	Amphotericin B	Streptomycetaceae	Amphotericin B	Antifungal
21.	*S. noursei*	Nystatin	Streptomycetaceae	Nystatin	Antifungal
22.	*S. pneuceticus*	Epirubicin	Streptomycetaceae	Doxorubicin, Epirubicin, Idarubicin	Lymphoma, breast cancer
23.	*S. rapamycinicus*	Nigericin	Streptomycetaceae	Rapamycin	Anticancer
24.	*S. roseosporus*	Daptomycin	Streptomycetaceae	Daptomycin	Blood, skin infections
25.	*S. rimosus*	Tetracycline	Streptomycetaceae	Oxytetracycline	Antibacterial
26.	*Streptomyces tenjimariensis*	Istamycin A, B	Streptomycetaceae	Istamycin A R1, Istamycin B R1	Antibiotic
27.	*S. thermophilus*	Gamma aminobutyric acid	Streptomycetaceae	Streptococcus thermophilus	Prevent young children from diarrhoea
28.	*Streptomyces tsukubaensis*	Tacrolimus	Streptomycetaceae	Tacrolimus	Immunosuppressant
29.	*S. venezualae*	Pikromycin	Streptomycetaceae	Chloramphenicol, Pikromycin	Antibacterial, Typhoid fever
30.	*S. verticillus*	Bleomycin	Streptomycetaceae	Bleomycin	Head and Neck cancer

Role of plants in drug development

Medicinal plants are used as a major source of drugs for thousands of years in human history and even at present times they are the basis of the systematic traditional medicine practices in many countries. The primary recorded literature on medicinal plants are often traced back to an earlier age of human history like the Atharvaveda (2000 BC) in India, the Divine Farmer's Herb- Root Classic (3000 BC) in China and therefore the Eber Papyrus (1550 BC) in Egypt. The modern drug industry has been developed to a substantial degree as a result of plant-based traditional medicines. A number of these plant-derived curative agents like atropine (anticholinergic), codeine (cough suppressant), colchicine (antigout), ephedrine (bronchodilator), morphine (analgesic) and physostigmine (cholinesterase inhibitor) are still being extensively used nowadays (Sneader, 1996). Active constituents extracted from plants can use directly as treatment in clinical use, like morphine, atropine, quinine and paclitaxel or as prototype biologically active "lead" compounds allow many structural analogs as new pharmaceutical agents like artemisinin and so the opiate derivatives. Besides their medicinal use some secondary metabolites from plants are also used as powerful "pharmacological tools" to help explain the mechanisms of basic human diseases (Principe, 1989; Cabnillas, 1979). Today drug discovery from plants is predicated mainly on bioactivity-guided isolation and groups of scientists with different research backgrounds including botany, biochemistry, pharmacology, pharmaceutics, pharmacognosy, medicinal chemistry, organic chemistry and toxicology are during this enterprise (Geisman 1969).

In addition to the biologically active plant-derived secondary metabolites which have been found to use as drug entities, many other bioactive plant compounds have proven usable as model compounds. β-carotene, a plant primary metabolite that can be useful within the prevention or treatment of various types of cancers. It is repeatedly forgotten that plant secondary compounds can use as templates for the design and total synthesis of the latest drug entities. For ex: belladonna alkaloids (e.g., atropine), physostigmine, quinine, cocaine, opiates (codeine and morphine), papaverine, and salicylic acid have served as models for the design and synthesis of anticholinergics, anticholinesterases, antimalarial drugs, benzocaine, procaine and other local anesthetics the analgesics pentazocine (Talwin), verapamil (Papaver and papaverine), and aspirin (acetylsalicylic acid), respectively. These examples and lots of others serve for instance the value and importance of plant-derived secondary metabolites as model compounds for contemporary drug development.

Conclusion

It may be concluded from this chapter that plants have vast uses in forming drugs for humans and animals. The survival of life highly depends upon various products extracted from these plants. Plant fulfills the need for foods, medicines, shelter, clothes and luxuries for humans. If the present trends of destruction and exploitation of forests continue at their present rates, scientists interested and involved in medicinal plant research may have only a couple of decades during which to investigate much of the rich diversity of the plant kingdom for useful secondary metabolites and lots of chances for successful drug invention will almost surely be lost.

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Chapter - 5
Plant Based Drugs: New Era for Cancer Treatment

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Chapter - 5

Plant Based Drugs: New Era for Cancer Treatment

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Abstract

Cancer is a major public health challenge. According to WHO 2020 report, 10 million death of people were listed as cancer. DNA damage triggered by ultraviolet radiations, environmental agents, ionizing radiations, etc. Almost all cancers are frequently diagnosed cancers are lung (12.7%), colorectal (9.7%), breast (10.9%), and gastric cancer (7.81%). Natural compounds are most favourable against cancer on their anti-cancerous ability, easy to avail and efficient. There is an urgent need for new effective anti-cancer drugs with fewer side effects, and plants show promising results for making drugs. In this chapter, we focus on some plant-derived drugs against cancer. These include 5-fluorouracil, artemisinin, polysaccharide, curcumin, etc. Also discussed uses and future prospects for the development of plant-derived substances with anti-cancer activity.

Keyword: anti-cancer, drugs, natural compounds, cancer

Introduction

Cancer is one of the deadliest ailments worldwide. It is one of the prime reason of deaths and morbidity round the world and is getting frequent increase in its cases and been expected to reach about 21 million by the end of 2030 [1, 2]. The reason now also includes the lifestyle change [3]. People are working hard to minimalize the destructing drug effects in the cancer therapy procedure on tissues and cells, and ultimately cumulating the lesion worth and drug growth for targeting systems and new drug distribution [4]. Several approaches are being used to treat cancer such as radiotherapy, chemotherapy, tumor surgery, cancer vaccinations, stem cell transformation, photodynamic therapy. But these therapies might include toxicity, fast clearance, non-specificity etc. [5, 6].

Plants are the good source for medicine from many years. Plant consists of many medicinal plants which are the finest source for developing drug. Hence, there's a serious need to search for some improved action for this

disease. We need to work on new agents because chemotherapy and radiation therapy which is widely being used for cancer treatment induce side effects on scale. The compounds obtained from plants are beneficial over the chemical ones as they are less or non-toxic to human and more endured. According many studies plants can constrain the sequence and expansion of cancer [3].

Action of plants showing anticancer property

The plants with anticancer activity include the polyphenols, flavonoids, alkaloids, saponins, triterpenes, tannins, and quinones. These bioactive compounds used as antiproliferative, cytostatic, cytotoxic, antimetastatic, apoptotic and antioxidative properties that inhibited angiogenesis and reduced cancer cell viability.

Polyphenols

Studies show that polyphenols have antioxidant and cytotoxic activities against cancer cells [7-9]. Polyphenols regulate the accumulation of copper ions on chromatin, stimulated by the polyphenols such as to elicit DNA disintegration, resveratrol [7].

Flavonoids

Natural flavonoids a wide class of polyphenolic compounds, chief sources of flavonoids are fruits, seeds, vegetables, beverages, and flowers, different type of foods has different quantity of anti-cancerous flavonoids. The known biological properties of natural flavonoids are anticipation against cancer, cardio-protective, inhibition of bone resorption and hormonal action. Flavonoids possess anti-inflammation, antioxidant, along with anti-cancerous activities through multiple pathways, they induce apoptosis in breast, colorectal, and prostate cancers. Flavonoids can also bind with the ATP-binding proteins including mitochondrial ATPase, protein kinase C, protein kinase A, calcium plasma membrane ATPase, and topoisomerase. The flavonoids delayed NF-κB expression. NF-κB is a protein complex required for the proliferation, angiogenesis and existence of cancer cells [10].

Alkaloids

The bioactive compounds disturbed tumorigenesis as well as the progression of tumor cell growth [11-13]. These bioactive compounds decrease cellular glutathione (GSH) levels by intermingling directly with GSH, hence stimulated the generation of ROS [15-18]. The alkaloids are complicated in the inhibition of NF-κB activation [11, 14].

Saponins

Saponins showed immunomodulatory activities through cytokine interaction [11]. Cytostatic and cytotoxic actions were shows the major anticancer mechanisms of saponins [19, 20]. The steroidal saponins promoted cancer cell cycle arrest and induced apoptosis, and acted as antitumor agents [21].

Triterpenes

Triterpenes such as 3-O-acetyl-11-keto-β-boswellic acid started tumor cell apoptosis over stimulation of the death receptor DR-5 signaling pathway [22, 23]. This class of bioactive compounds induced tumor angiogenesis by preventing the emission of the angiogenic factors: VEGF-A and bFGF and the vascular endothelial growth factor [24, 25]. The cancer cell triggering enzymes, proteins, and signalling pathways like CDK2, CDK4, Cdc2 kinases cyclooxygenase, topoisomerase enzyme, COX-2(cyclooxygenase), PI3K, Bcl-2, cytokines, Akt, MAPK/ERK, TNK, MMP could be achieved by most the plants products like as flavonoids, saponins, vitamins, taxanes, alkaloids, oils, minerals, gums etc which triggers DNA repair procedure (p53, p21, p51, p27 genes and commodities of protein by targeting the rapamycin. (Figure1) [26].

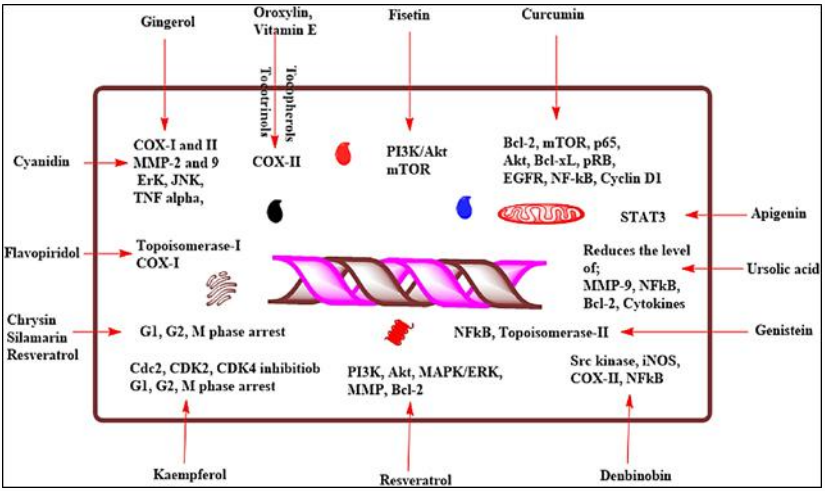

Fig 1: Impact of anticancer phytochemicals after activating expression of various genes, proteins, enzymes and signaling cascades in order to block cancer initiation and progression [26]

Certain proteins like BAX, BAK, Bid tempts antioxidant effect, protective enzymes development (Caspase-3, 7, 8, 9, 10, 12) and hence display strong anticancer effects and worthful on proteins, enzymes and signalling pathways (Figure-2) [26-28].

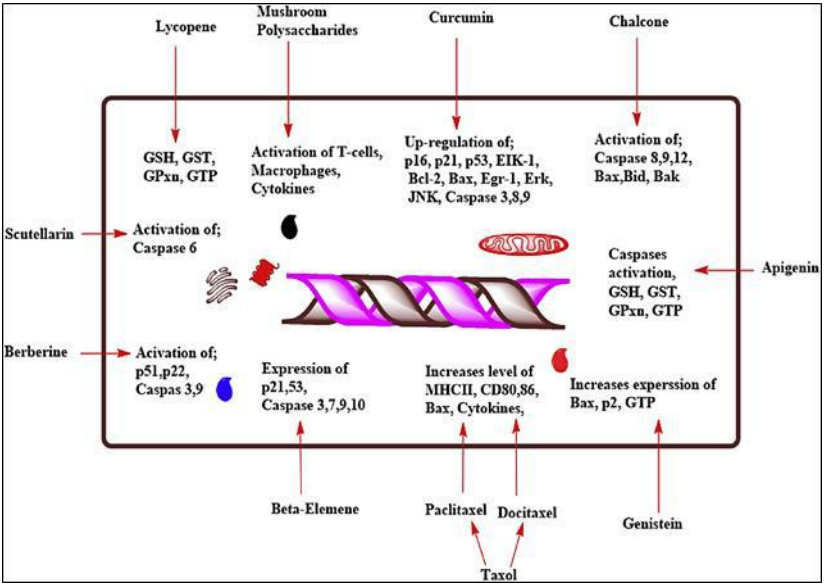

Fig 2: Impact of anticancer phytochemicals after inhibiting expression of various genes, proteins, enzymes and signaling cascades in order to block cancer initiation and progression [26]

After going through the certain researches, we found that there are many plants that shows anti- cancerous activity as follows-

S. No.	Plant	Common Name	Component	Cancer	Reference
01	*Zingiber officinale*	Ginger	Ginger	Ovary, cervix, colon, liver and urinary caner.	[29]
02	*Withania somnifera*	Ashwagandha	5-Fluorouracil	Human cervical cancer cell.	[30]
03	*Artemisia annua*	Sweet wormwood, sweet annie and sweet sagewort	Artemisinin	Breast cancer	[31]
04	*Astragalus membranaceus*	Mongolian milkvetch	Polysaccharide	Liver cancer	[32]
05	*Curcuma longa*	Turmeric	Curcumin	Colon cancer	[33]
06	*Garcinia indica*	Kokum	Garcinol	Colon cancer	[34]
07	*Rabdosia rubescens*	Bing Ling Cao, Blushred Rabdosia and Isodon Rubescens	Oridonin	Gallbladder cancer	[35]

08	*Tinospora cordifolia*	Guduchi	Dichloromethane	Brain tumor	[36]
09	*Plumbago zeylanica*	White leadwort, chitrak and Ceylon leadwort	Naphthoquinone	Prostate cancer	[37]
10	*Colchicum autumnale*	Autumn crocus	Colchicine	Hodgkin's lymphoma, chronic granulocytic leukemia.	[38]

In our paper our major focus is on one plant *Curcuma longa.*

Curcuma longa

Curcumin is the most important component of the rhizomes of *Curcuma longa* L. (turmeric) [39]. The current literature has found that new anticancer mechanism for curcumin by inhibiting the lactate production (Warburg effect) glucose uptake and in cancer cells by downregulation of pyruvate kinase M2 (PKM2). The inhibition of PKM2 was achieved by defeating the mammalian target of rapamycin-hypoxia-inducible factor 1α (TOR-HIF1α) [40]. Studies shows the ability of curcumin and its derivatives to defeat multiple different carcinomas by networking with different molecular targets (figure. 3) [41].

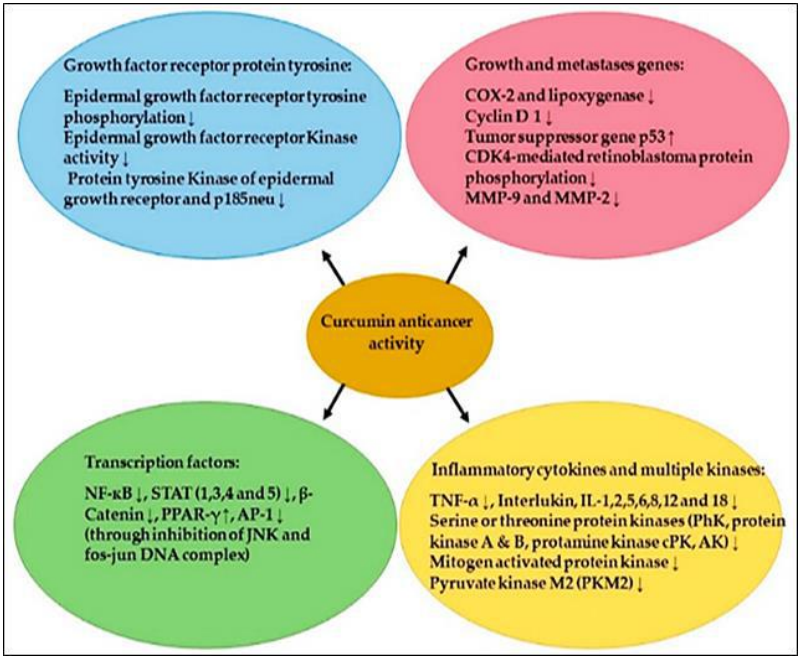

Fig 3: Molecular targets of curcumin in cancer cells. ↑: Increase; ↓: Decrease; MMP: Matrix metalloproteinase; AP-1: Activation pro1 [41]

Both *in vitro* and *in vivo* studies show that curcumin has strong capability to induce apoptosis and inhibit proliferation in prostate cancer [42] by interfering with cellular pathways, including epidermal growth factor receptor (EGFR), nuclear factor κ (NFκB) and mitogen-activated protein kinase (MAPK) [43, 44].

A current study says the ability of curcumin to activate protein kinase D1 (PKD1), leading to a decrease in the oncogenic signalling by MAPK and catenin and resulting in inhibition of prostate cancer. Likewise, PKD1 was found to be down structured following progression from androgen-independent from androgen-dependent prostate cancer [45] and E-cadherin affects the invasion and motility of prostate cancer [46] and considered as a new therapeutic target for prostate cancer [47]. Studies show that Dimethyl curcumin (ASC-J9) shown good results in androgen-dependent prostate cancer by enhancing androgen receptor degradation [48, 49].

After prostate cancer and lung cancer, colorectal cancer is the most common form of cancer [50]. After diagnosing this cancer removed by surgery and chemotherapy, most of the patients suffer from relapses [51]. Studies found that to reduce M (1) G levels without changing COX-2 protein levels in the malignant colorectal cells [52].

In vitro research of curcumin in different head and neck cancer cell lines has confirmed its ability to inhibit cell growth that affects cellular pathways involved in cell propagation, especially STAT3 and NF-κB, which are overexpressed in some neck and head carcinomas [53, 54]. Curcumin remained shown downregulate NF-κB and suppress the interleukin-6 (IL-6)-mediated phosphorylation of STAT3, thus inhibiting the cancer cells [54, 55].

In research on MCF-10A human mammary epithelial cells and MCF-7 breast cancer cells, telomerase activity was observed in tangible drops as a consequence of treatment with curcumin in a concentration-dependent manner which was associated to downregulation of Telomerase reverse transcriptase (hTERT) via curcumin but not with the c-Myc mRNA pathway [56]. In contrast with the previous literature, this study showed curcumin's ability to downregulate NF-κB, leading to an antiproliferative effect with breast cancer cell lines [57, 58]. Dimethyl curcumin (ASC-J9) has also been reported to be effective against inhibiting several types of steroid receptors in estrogen-dependent breast cancer [59, 60].

Therefore, alternative therapies using naturally derived compounds such as curcumin shows promising results and fewer side effects via conventional treatment. Curcumin has shown multiple molecular targets (Figure. 3),

consequently, combating brain tumours may take different cellular pathways autophagy, including apoptosis, invasion, angiogenesis, and metastasis [61].

Future of plant-based drugs

Subsequently, from primordial time turmeric is the most basic and significant medicine in Ayurveda, and currently scientists are showing keen interest in bringing the treatment of diseases from plant based natural products. Studies are still in progress but not exactly a drug development have been carried out till now. In case of curcumin, it is vastly auspicious antioxidant and non-hazardous. Curcumin is easily available and can be tested properly to develop drug for studying its action mechanism and medicinal effects. It is believed that Curcumin has a very wide purpose in novel drug to regulate different diseases, oxidative stress and disorders.

Conclusion

Cancer is one of the most dangerous problem around the globe. Many therapies are also been practised to treat cancer. But as these therapies utilise chemical compounds, they exhibit many long-term side-effects too. Hence, here in our paper we are reviewing about the use of plants for treating this disease which are even less toxic to human beings and plant based organic compounds like alkaloid, flavonoids etc are used for this purpose. There are so many plants showing anticancerous effects but in our review the major focus is on *Curcuma longa.* We chose this plant as it exhibits antioxidant. Anti-inflammatory, and anticancer effects. This plant has shown effects over breast cancer, pancreatic cancer, neck and hand cancer etc. After going through the latest research, we went to the conclusion that *Curcuma longa* has highest drug efficacy and few varied effects. Although there are certain alterations that makes it difficult to increase its efficacy but working in it might help us in overcoming this event.

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Chapter - 6
Recent Approaches for Plant-Derived Drug Discovery

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Chapter - 6

Recent Approaches for Plant-Derived Drug Discovery

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Abstract

At present, challenges before the world to develop and maintain our available natural resources-based technologies specially related to drug discovery approaches in the context, over growth of population and over exploitation of natural resources. In India, the plants use in a therapeutic healing both traditionally and medicinally up to ancient periods. In Charak samhita, 340 drug origin from vegetable plants species used for the therapeutic treatments of human's disease. The locally available plant has a much and more medicinal values we have collect these literatures and summarized in this type of plant and highlight their medicinal capacity and combinations for the recent approaches of drug discovery. Already isolated drug and their therapeutic combination shown in table-1, and in the table-2 shown various part of the plants use in treatments and table-3 shown various plants locally people use in antiviral activates recent Covid-19 pandemic duration, after that discovered have two vaccines, Covaxin and Covisheild to empirical cure or a vaccination for this potentially fatal disease. Mention traditional and current technical methods for recent approach plants drug design, highlight positioning and repurposing for drug and its outlines charts. The pharmacological uses of plants and diagrammatic shown the chemical structure of primitive and modern drug compound and molecules. The material is used for the study and research regarding fields.

Keywords: Ayurveda, Covaxin and Covisheild, drug-repositioning, drug-discovery, herbal-medicines, compound, therapeutic agent, natural-products

Introduction

Systematic and practical medical knowledge in India is called Ayurveda. Medicinal knowledge gained over trial and error over the thousands of years in India and neighboring regions of Asia/south Asia has been systematized some four thousand years ago in a system of medicine called Ayurveda. Ayurveda (pronounced, I-your-vay-da), the science of life prevention and

longevity is the oldest and most holistic or comprehensive medical system available. It was placed in written from over 2000 year ago in India, it is said to be a world medicines before the advent to writing, the ancient wisdom of healing, prevention and longevity was a part of the spiritual tradition of a universal religious. Medical knowledge from all area of the world gathered in India and the famous sage Vyasa, put into writing the complete knowledge of Ayurveda along with the more directly spiritual insights of ethics, virtue and self-realization. In Ayurvedic the method used to acute this knowledge of the uses of herbs, foods, aromas, gems, colors, yoga mantras lifestyle and surgery. the sage physician or surgeon of the time were the same sages or seers, deeply devoted holy people who saw health as an integral part of spiritual life. it is said that they received their training of Ayurveda through direct cognition during meditation. In other words, the knowledge of the use of the various methods of healing, prevention, longevity and surgery come through divine revelation; there was no guessing of testing and harming animals. These revelations were transcribed from the oral tradition into book from interspersed with the other aspects of life and spiritually.

The vedas: Rik, Soma Yajur and Atharva. Ayurveda was used in conjunction with Vedic astrology (Jyotish-inner light). Ayurveda was organized into its on compact system of health and considered an auxiliary branch of the Vedas called an Upaved (Limb of the Veda), because it dealt with the healing aspect of spiritually, and not directly discussing spiritual development. Ayurveda from the various Vedas and made separate books, dealing only with; Ayurveda. Among the Rik Veda's 10,572 hymns, are found discussion of the three doshas Vayu, Pitta, Kapha: organ transplant and artificial limbs the use of herbs to heal the disease of the mind and body and to faster longevity. within the Atharva Veda's 5,977 hymns, are discussion of anatomy physiology and surgery. Around 1500 B.C. Ayurveda was delineated into eight specific branches of medicines. There were two main school of Ayurveda at that time Atreya-the school of physicians; and *Dhanvantari*-the school of surgeon.

Origin ethics: The origin of this system of course is lost in time. In legend it is said to have been taught by the creator to the Prajapati Daksh (one of the lards of animals) who taught to the divine twins called the Aswins.

Great concept of Ayurveda: Vyaadhi or disease in Ayurveda is due to an imbalance of three fundamental element of the body. These are VATA, PITTA and KAPHA. The entire universe is made of five *Mahabhootas* or

great elements these are called; 1. Akaasa (space) 2. Vaayu (air) 3. Tejas (light) 4. Ap (water) 5. Prithvi (earth).

Description of this thee Vaata, Pitta and Kapha.

The Vaata: Humans body are mainly made of AkasaVaayu, with a little of Teja, Ap and Prithvi. Vaata is what allow one to interact with environment. Briefly vaata transmit sense impression to the mind and response to various place of the body maintain the integrity of the body and proper functioning of its various constituent elements the sensory organ of touch and sound depend on Vaata.

The Pitta: In the primary constituents of the living body whose structure is Tejas (luminouslight) its function is balancing and transformative. Its function in particular are-"vision, digestion, production of heat, hunger, thirst softness and suppleness of body, lustre, cheerfulness and intelligence.

The Kapha: Is one of the primary constituents of body having "water" and "earth" as elements. Function of pitta is conserving and stabilizing. It organizes the tissue.

Influence of Ayurveda: Other system of medicines such as chine's, Tibetan and Islamic tradition have their roots in Ayurveda. The buddha born 550 B.C. was follower of Ayurveda and spread of Buddhism into Tibet during and Buddhism countries. The ancient civilization was liked to one another by trade ruts campaign and war Arab trade spreads knowledge of Indian plants and Ayurvedic was studied by Arad physicians who include Indian plant and their Material Medica, and the knowledge was spreads on the ancient Greek and Romans.

Foreign herbs and synthesized drugs

The growing use of foreign herbs in the 17th prompted heated debate about the relative value of indigenous European herbs, but for the majority of the population this was irrelevant as the imported herb were well out of their price range. Herbal medicine uses rural people used locally while affluent city dwellers and aristocrats purchased plants foreign origin, prescribed by university-trained physicians. In beginning of 18th century approximately 75 percent of plants medicines stock by European countries were imported. In the 19th century it becomes to practice herbalists known as Komboyannites, were persecuted.

In India

The name Ayurveda derived from two Indian words; *ayur* meaning life and Veda means knowledge of science. Ayurvedic medicines is more than a

system of healing. It is way of encompassing science, religious and philosophy that enhance well -being, increased longevity and ultimately self-realization. it aims to bring about a union of physical, emotional and spiritual health known as Swasthya.

In China medicines

Uses of traditional Chinese medicines of the herbal tradition the part of developed separately for Chinese folk medicines. Its tradition for thousands of years. Its idea recorded between 200 BC. and AD.100 in the yellow Emperor's.Encyclopedia of tradition Chinese medicinal substance which has about 5,757 and most of them are herbs. The communist revolution in 1949 help the swell number of plants used in traditional Chinese medicines, uses mainly for chronic condition. Because herb that had previously only employed in folk medicines. Influence by idea of traditional Chinese medicine in Japan and Korea.

New frontiers and herbal medicines

European settled during the great migration of the 18^{th} and 19^{th} centuries-North American, South, America, Southern Africa or Australia-much of the European medicine familiar from home was either unavailable or prohibitively expensive. Settler came to learn that native people were a wellspring of information about the medicine virtues of indigenous plants. For example, European settlers in southern Africa learned about the diuretic properties of *Buchu (Barosma betulina)* from native peoples and Australian shelters came to understand the remarkable antiseptic properties of tea tree (*Melaleuca alternifolia)* from observing the medicine as it exists today is a bland of Aztec, Mayan and Spanish herbs and practices. In northern America, Native herbalist were particularly adept at healing external wounds and bites, being superior in many respects to their European counterparts to their area of medicine. This is not surprising given the range of highly effective medicinal plants native American had discovered including well known herbs such as Echinacea (*Echinacea angustifolia)* goldenseal (*Hydrastis canadensis*) and lobelia (*Lobelia inflata*)

Brief history of the plant utilization

History of the plant one most go back to the history of utilization of plant and pharmacology for until the last century medicinal plant were still being process for general use. The history of discovery of the curative and therapeutic prosperities of plant these are must have sprung from some human instinct uses. Primitive man used plants for the food and medicine. He would have learnt after perhaps many unfortunate experiences that some

plant contained curtained prosperities and able to identify them by the results they induced. He would also have observed which plants animals utilize when they were sick. After seeing an injured deer robbing itself against the geom. He might have discovered for instance they this plant would hell his own wounds and realized that dog tooth grass would act as an emetic as it did with the cat. Many remarkable example of animal institutively knowing how to treat with appropriate plants are quoted by numerous writers Cicero for example mentioned.

Early origin of the 19 Century

Medicinal plants have been maintained to sustainable the health and well-being of mankind. Humans knew the importance of linseed oil *Linum usitatissimum* oil as nutritious cooking oil, fuel, a cosmetic balm for the skin and treatment of some disease's bronchitis, respiratory and digestion disorders. 60000, years old burial site excavated in Iraq to be found different medicinal plants, for the medicinal purpose including *Ephedra* plant. In many civilizations' plants were considered to have souls. Even Aristotle, the 4th, century BC Greek Philosopher, through the plant had a psyche, albeit of a lesser order than the human's soul. In medieval Europe the doctrine of signature stated there was a connection between how a plant looked Gods, signature and how it might be used medicinally for example the mottled leaves of lungwort (*Pulmonaria officinalis*), were thought to resemble lung tissue and the plant is still used to treat ailment of the respiratory tract. Similar in western culture it is a belief that plant sprits linger. In Britain people do not cut down elder trees for fear of arousing the anger of the elder mother the sprit that lived in and protected the tree. In Hindu culture plant are sacred to specific divinities. For example, the bale tree *Aegle marmelos* is said to s helter "Lard Shiva, the God of health, beneath and branches. In South America believe that the coca plant (*Erythroxylon coca*) is protected by Mama Coca, a sprit who must be respected and placated it the leaves are to be harvested and used. In many traditions' societies illness is through to stem from malignant plant have healing power. In Egypt the Middle East India and China civilization grew from 3000 BC. On words therefore the use of herbs becomes more sophisticated. They made first written account of medicinal plants.

In India, the Vedas the epic poem had written 1500 BC. This volume contended rich material on herbal lore of that time. The Vedas were followed in about 700 BC. By the Charaka Samhita, written by the physician Charaka. He is known as is known Father of medicine of India. This medical treatise includes details of around 350 herbal medicines. Amongst them are Visnaga

(*Ammi visnaga*) an herb of middle east Eastern origin that has recently proven effective in the treatment of asthma and Gotu, kola (*Centella asiatica*) which has been long used to treat leprosy.

Indian Islamic medicine AD500-1500

In the Arabic culture AD. 500-1500 gained the classical Greek and Roman ideas for medicinal plants. They preserved and elaborated them. The spread of Islamic cultural along North Africa and present Day Italy, Spain and Portugal led to the founding of renowned medical schools notably at Cordoba in Spain. The Arabs were expert pharmacist, blending and mixing herbs to improve their medicinal effects and their tastes. Their contract with both Indians and Chinese medical tradition meant that they had remarkable range of medical and herbal knowledge to draw on and develop.

Medical plants in European countries AD-1000-1400

The classical Greek Roman and Egyptian literature were preserved in the libraries of Constantinople which filtered back to Europe. This encouraged European scholar to established hospitals medical scholars and universities the medical school at Salerno on the west coast of Italy is one of the prime institutes. It not only allowed from all faiths-Christian Moslem and Jewish- to study medicine but it also allowed women to train as physicians. In 12^{th} century, trade with Asia expanding and new herbs species were being regularly imported into Europe. Hildegard of Bingen (1098-1179) the famous German mystic and herbal authority, considered galangal (*Alpinia officinarum*), used in Asia as a warming and nourishing spice for the digestive system-to be the "spice of life "given by God to provide health and to product against illness.

Development in Asia

Macro Polo's travels to China in the 14th century coincided with the unification of the whole of Asia from the Yellow Sea in China to the Black Sea in South-eastern Europe by Genghis Khan and his grandson Kublai Khan, whose capital was in China, not far from Beijing. Neither the Chinese nor Ayurvedic medicine medical tradition were directly threatened by this conquest. The ruler of Mongol tried to stop use of a few toxic plants like aconite (*Aconitum napellus*). The people were using aconite as alternative of arrow poison-one that could have been used against the ruling powers. Mongols have tried to make unification between the two medical disciplines. In other part of Asia, such Vietnam and Japan, Chinese culture and medicine exerted the primary influence. While kampo-the traditional herbal medicines of Japan are distinctive to that country.

The trading of medicinal plants

In 15th century onwards an explosion in trade led to a cornucopia of a new herbs becoming readily available in Europe. They include plants such as ginger (*Zingiber officinalis*) Cardamom (*Eletoria cardamomum*) nutmeg *Myristica fragrans* turmeric (*Curcuma longa*) cinnamon (*Cinnamomum verum)* and senna (*Cassia senna*) the trade is herb was not entirely one way. The European herb sage the example come into use in China where it was considered to be a valuable yin tonic. In 1942 ships of Columbus arrived in the Caribbean which was followed in the rapid conquest and colonization of central and South Africa by the Spanish and Portuguese. Along with their booty plundered gold the conquistadores returned to the old world with previously unheard-of medicinal plants various herb from the Americans had highly potent medicinal action. They soon become available in the apothecaries of the major European cities. Plant such as lignum vitae (*Guaiacum officinale)* cinchona were used for treatment of fever malaria, syphilis, smallpox and other serious illness. The natural communities tried to foreign plants for medical and food valve. In the other country's Potatoes (*Solanum tuberosum*) and Maize both native to south America become common food for all. These plants clear medical as well as nutritional benefits. Potato juice is a valuable remedy for arthritis, while corn silk makes effective decoction problem such as cystitis.

1.1 Identified plants drug and their chemical compounds.

The plant use as a foods and medicines about 6-7% of the out of 250000 angiosperms plants but some plants have extra potentially capacity for the therapeutic treatment for many humans' disease those are screening by some surveyor. Most of the observer about 15-20% have been evaluated for phytochemically. These are all useable plants identified and screened for the therapeutic and ayurvedically useable. Plants have an advantage this area based and their long-term use by the humans expect any bio active compounds obtained from such plant to maintained and minimize toxicity. Some plants may be toxic within a given endemic pandemic culture that have no reporting system of these effects. Plants have much medicinally properties we should try and attempt this to modified and converted as a useable therapeutic use for the particular diseases, most of the large pharmaceutical manufacturer and biotechnological Industries and drug company able to screening for identified plants uses as a therapeutic medicine it is thousand and more plants to identified and isolate for their valuable biochemicals but the challenges of the all these firms forthcoming viral pandemics. Most of the important plant drugs occur and isolates by the following plant.

Table 1: Drugs derived from plants, with their ethnomedical importance and sources

Drug	Action or Clinical use	Plant Source
Acetyldigoxin	Cardiotonic	*Digitalis lanata* Ehrh
Adoniside	Cardiotonic	*Adonis vernalis* L.
Aescin	Anti-inflammatory	*Aescus hippocastanum* L.
Aesculetin	Antidysentery	*Fraxinus rhynchophylla* Hance
Agrimophol	Anthelmintic	*Agrimonia eupatoria* L.
Ajmalicine	Circulatory disorder	*Rauvolfia serpentina* (L) benthex Kurz
Allyl isothiocyanate	Rubenfacient	*Brassica nigra* (L) Koch
Andrographolide	Bacillary dysentery	*Andrographis paniculate* Nees
Anisodamine	Anticholinergic	*Anisodus tanguticus* (Maxim) Pascher
Anisodine	Anticholinergic	*Anisodus Tanguticus* (Maxim) Pascher
Arecoline	Anthelmintic	*Areca catechu* L.
Asiaticoside	Vulnerary	*Centella asia cica* (L) Urban
Atropine	Anticholinergic	*Atropa belladona* L.
Berberine	Bacillary dysentery	*Berberis vulgaris* L.
Bergenin	Antitussive	*Ardisia japonica* BL.
Bromelain	Anti-inflammatory; proteolytic agent	*Ananas comosus* (L.) Merrill
Caffeine	CNS stimulant	*Camellia sinensis* (L.) Kuntze
± Catechin	Haemostatic	*Potentilla fragaroides* L.
Chymopapain	Proteolytic; mucolytic	*Carica papaya* L.
Cocaine	Local anaesthetic	*Erythroxylum coca* Lamk.
Codeine	Analgesic; antitussive	*Papaver somniferum* L.
Colchicine	Antitumor agent; antigout	*Colchicum autumnale* L.
Convallotoxin	Cardiotonic	*Convallaria majalis* L.
Curcumin	Choleretic	*Cucurma longa* L.
Cynarin	Choleretic	*Cynara scolymus* L.
Danthron	Laxative	*Cassia* spp.
Deserpidine	Antihypertensive; tranqualizer	*Rauwolfia canescens* L.
Deslanoside	Cardiotonic	*Digitalis lanata* Ehrh.
Digitalin	Cardiotonic	*Digitalis purpurea* L.
Digitoxin	Cardiotonic	*Digitalis purpurea* L.
Emetine	Amebicide, emetic	*Cephaelis ipecacuanha* (Brotero) A.

Ephedrine	Sympathomimetic	*Ephedra sinica* Stapf.
Etoposide	Antitumor agent	*Podophyllum peltatum*
Gitalin	Cardiotonic	*Digitalis purpurea* L.
Glaucaroubin	Amoebicide	*Simarouba glauca* DC.
Glycyrrhizin	Sweetener	*Glycyrrhiza glabra* L.
Gossypol	Male contraceptive	*Gossypium* spp.
Hemsleyadin	Bacillary dysentery	*Helmsleya amabilis Diels*
Hydrastine	Hemostatic; astringent	*Hydrastis canadensis* L.
Hyoscamine	Antichlinergic	*Hyoscyamus niger* L.
Kainic Acid	Ascaricide	*Digenea simplex* (Wuif) Agardh
Kawain	Tranquilizer	*Piper methysicum* Forst. f.
Khellin	Bronchodilator	*Ammi visnaga* (L.) Lamk.
Lenatosides A.B.	Cardiotonic	*Digitalis lanata* Ehrh.
Lobeline	Smoking deterrent; Respiratory stimulant	*Lobelia inflata* L.
Monocrotaline	Antitumor agent	*Crotalaria sessiliflora* L.
Morphine	Analgesic	*Papaver sominiferum* L.
Neoandrographolide	Bacillary dysentery	*Andrographis paniculata* Nees
Noscapine	Antitussive	*Papaver sominiferum* L.
Ouabain	Cardiotonic	*Strophanthus grantus* Baill.
Papain	Proteolytic, mucolytic	*Carica papaya* L.
Phyllodulcin	Sweetener	*Hydrangea macrophylla (thumb)*
Physostigmine	Cholinestares inhibitor	*Physostigma venenosum* Balf.
Picrotoxin	Analeptic	*Anamirta cocculus* (L.) W&A
Pilocarpine	Parasimpathomimetic	*Pilocarpus jaborandi* Holmes
Podophyllotoxin	Cardylomata acuminata	*Podophyllum peltatum* L.
Protoviratrines	Antihypertensive	*Veratrum album* L.
Pseudoephedrine	Sympathomimetic	*Ephedra sinicastapf.*
Quinine	Antimalarial	*Cinchona lendgeriana* Moens ex. Trimen
Quisqualic acid	Anthelmintic	*Quisqual indica* L.
Reseinnamine	Antihypertensive tranquliser	*Rauvolfia serpentina* L. benth ex. Kurz
Reserpine	Antihypertensive tranquliser	*Rauvolfia serpentina* L. benth ex. Kurz
Rhomitoxin	Antihypertensive	*Rhododendron mole* G. Don
Rorifone	Antitussive	*Rorippa indica* L.
Rotenone	Piscicide	*Lonchocarpus Nicou* (Abul)
Rotundine	Analgesic sedative	*Stephania sinicadiels*

Salicin	Analgesic	*Salix alba* L.
Santonin	Ascaricide	*Artemisia maritima* L.
Scillarin A	Cardiotonic	*Urginea maritima* L. Baker
Scopolamine	Sedative	*Dhaturametel* L.
Sennosides A &B	Laxative	*Cassia* spp.
Silymarin	Antihepatotoxic	*Silybum marianum* L. Gaertn
Stevioside	Sweetener	*Stevia rebaudiyana* Bertoni
Strychinine	CNS stimulant	*Stychnosnux vomica* L.
Teniposide	Antitumor agent	*Podophyllum peltatum* L.
Tetrahydropalmatine	Analgesic sedative	*Coridali ambigua* (pallas)
Theobromine	Diuretic bronchodilator	*Theobroma cacao* L.
Theophylline	Diuretic bronchodilator	*Camellia sinensis* L. kuntze
Trichosanthin	Abortifacient	*Thymus vulgaries* L.
Tubocurarine	Skeletal muscle relaxant	*Chondrodendron tomentosum*
Valepotriates	Sedative	*Valeriana officinalis* L.
Vincamine	Cerebral stimulant	*Vinca minor* L.
Xanthotoxin	Leukoderma vitiligo	*Ammi majus* L.
Yohimbine	Aphrodisiac	*Pausinystalia yohimbe*
Yuanhuacine	Abortifacient	*Daphne genkwa* Seib & Zuce

The use of plant as a medicine for the therapeutic uses could be called more accurately ethnobotanic medicines and Ethnomedicinally may be defined as broadly and ethnopharmacology is a high diversified drug discovery approach through the identification, observation, description, experimental and investigation of indigenous drug discovery. The basic criteria and involve discipline like botany, chemistry biochemistry, pharmacology and others importance's. Medicinal herbs are blessings from nature towards entire humankind, which provide timely and adequate remedies to several human's health disorders. Medicinal herbs allow people to increase their immunity in times of health problem like novel coronavirus in pandemic periods. It is evident from the human history that medicinal plants have been the treatment to cure a variety of diseases, including diseases caused by, bacteria, viruses. Fungi and insects the effects shown by the plants are due to the chemicals present in them, and they work in the same manner as conventional therapeutic drugs. In the present time, we need to understand the correlation between medicinal plants, immune systems, and Covid-19. Recently, the world health organization (WHO) estimated that 80 percent of people worldwide esthetical depends on medicinal herbs for their primary health care their needs. According to the WHO, around 21,000 plant species have the potential to be used as medicinal plants. Medicinal

plants and the immune system: Scientists have focused on preventive measurements and explored fast health remedies. Many of the plants & herbal extract in the form of *alkaloids, terpenoids, flavonoids, polysaccharides, glycoside and lactone* products are responsible for causing alterations to the improved, boosting immunological responses. Ayurveda experts have emphasized that medicinal herbs such as Aswgandha, *Withania somnifera, Glycyrrhiza glabra, Tinospora cordifolia, Andrographis paniculata, Piper nigram* etc. are advantageous in boosting the immune system to combat against the deadly viruses. Severe acute respiratory syndrome produces coronavirus-2 (SARS-CoV-2) that causes novel corona virus disease 2019 (Covid-19), primarily effects on the lungs and the respiratory tracts. The valuable prosperities of some therapeutic medicinal plants given below summarizes with special reference to immunological responses (Table-2).

Botanical name	Common name	Family	Uses
1. Root and other underground part. *Acorus calamus*	Sweet flag	Araceae	Antispasmodic, expectorant and carminative, used in epilepsy and other therapeutic uses sedative and analgesic.
Ferula asafoetida	Hing	Apiaceae	Source of the gum-resin, *Ferula asafoetida*, useful in the treatment of asthma cough and indigestion disease.
Rauvolfia serpentine	Sarpagandha	Apocynaceae	The drug *Rauwolfia serpentina* is used for relief from nervous disorder and anxiety states, excitement, maniacal behavior associated with psychosis, schizophrenia, insanity, insomnia, and epilepsy; used in high blood pressure and hypertension treatments.
Colchicum autumnale	Hirantutiya	Liliacea	Yields colchicine's, carminative, Laxative, and aphrodisiac; used in gout, rheumatism and disease of liver and spleen treatment.
Cephaelis ipecacuanha	Ipecacunha	Rubiacea	Emetic, diaphoretic, and expectorants, useful for the disease of allaying cough and catarrhal affections, and irritable conditions of the membrane of urinary organs.
Panax schinseng, P. guigue-folium	Ginseng	Araliacea	Disorder of stimulants, stomachic, demulcent and expectorant and antipyretic, influences metabolic and prevents development of arthrosclerosis.
2. Bark *Podophyllum hexandrum, P. peltatum*	Podophyllum	Berberidaceae	The plant drug Podophyllum is therapeutic used as a purgative and an effective vermifuge also used for tumorous growth.
Rheum officinales	Rhubarb	Polygonaceae	Used as a purgative and astringent tonic stomach disorder.
Myrica esculenta	Kaiphal	Myriaceae	Astringent, carminative and antiseptic; useful in asthma, diarrhea, fevers, chronic bronchitis, lung affections and dysentery and dieresis and disorder.
Bauhinia variagata	Kachnar	Caesalpiniaceae	Plant extract tonic and anthelmintic; used in scrofula and cutaneous troubles; also used for ulcers and leprosy disease.

Rhamnus purshiana	Cascara	Rhamnaceae	Plant extract use in tonic and laxative.
3. Stem and wood *Ehedraequistina, E. sinica*	Ephedra	Ephedraceae	Plant drug source of ephedrine; given for asthma and other respiratory troubles.
Ferula galbaniflua	gandhabiroja	Apiaceae	Source of galbanum; used for the stimulants, carminative, expectorant, and antispasmodic.
Santalum album	Safed chandan	Santalaceae	Uses in Diuretic, diaphoretic, refrigerant and expectorant, used as a sedative and cardiac tonic.
4. Leaves *Atropa belladonna*	Belladonna	Solanaceae	Used in the sedative, antispasmodic, and anodyne; used in ophthalmology to dilate pupil.
Adhatodavasica	Vasaka	Acanthaceae	The plant drug Vaska is used in bronchial troubles and consumption; also used in diarrhea, dysentery, glandular tumors and skin affections and others.
Aloe barbandensis	Ghee-kunvar	Liliaceae	This plant uses cathartic and refrigerant; used in liver and spleen ailments and for eye troubles; found useful in x-ray burns, dermatitis, cutaneous leishmaniasis and other skin disease and disorder.
Digitalis purpurea	Foxglove	Scrophulariaceae	The medicines Digitalis is used as a cardiac stimulants and tonic; increase the force of systolic concentration and the efficiency of decompensate heart. It is a diuretic useful in renal obstruction and dropsy disease**.**
Hyoscyamus niger	Khurasani Ajwain	Solanaceae	Plant drug Henbane has anyone, narcotic and mydriatic properties; employed as a sedative in nervous affections and irritable condition, such as asthma and whooping cough.
Mentha arvensis, M. pipertia M. longifolia	Pudina	Lamiaceae	Uses in stimulants and carminative, used for allaying nausea and flatulence, and externally applied in rheumatism, neuralgia, congestive headache, and toothache etc.
Holarrhena antidysenterica	Kurchi	Apocunaceae	Plant Astringent, anthelmintic, stomachic, antipyretic, tonic and antidysentery used in amoebic dysentery diarrhea disease.
5. Flowers	Laung	Myrtaceae	Pant dried unopened floral buds, known as ‘Clove’, are used as aromatic,

Syzygium aromaticum			stimulants and carminative; used for dyspepsia and gastric irritation and inflammatory.
Artemisia maritime	Wormseed	Asteraceae	The plant drug used as an anthelmintic, particularly effective against roundworm; stomachic laxative and febrifuge effects.
Leucas cephaloes	Dronapushpi	Lamiaceae	Treatment of stimulants, diaphoretic, laxative and anthelmintic used for cough and cold.
6. Fruits and seeds *Papaver somniferum*	Opium poppy	Papaveraceae	The famous plant drug emollient, demulcent, and laxative used in chronic constipation, dysentery and diarrhea, and inflammatory condition of gastrointestinal and genitor-urinary tract. Poultice of crushed seeds applied to rheumatic and glandular swelling disorder.
Strychnosnux-vomica	nux-vomica	Loganiaceae	Medicines used as a tonic, stimulants and febrifuge; also used in preparation for nervous disorder.
Plantago ovate	Isubgol	Plantaginaceae	These are use emollient, demulcent and laxative; and chronic consumption, dysentery and diarrhea and inflammatory condition of gastrointestinal and genitor-urinary tract. Poultice of crushed seeds applied to rheumatic and glandular swellings disorder.
Junipers communis	Haubera	Cupressaceae	The plant drug carminative, stimulants and diuretic, used in dropsy, disorder of urinogenital tract cutaneous disease and disorder.
Croton tiglium	Jamalgota	Euphorbiaceae	Plant drug used as a violent purgative and vesicant.
Chenopodium ambrosioides var. anthelminiticum	American wormseed	Chenopodiace	Medicine used as an anthelmintic, especially for hookworm infections disease.
Strophanthus hispidus	Strophanthus	Apocynaceae	Plant drug used as cardiac stimulant.
Taraktogenos Kurzii	Chaulmugra	Flacourtaceae	Plant drug used as an external application in leprosy.
Citrulina colocynthis	bitter apple	Cucurbitaceae	Plant uses as drastic hydragog, cathartic.
Piper cubeba	Kababchini	Piperaceae	Used for the aromatic stimulants, local irritant, durotactic, carminative and sedative; used in rheumatism, gonorrhea, bronchial troubles etc.

Many plants derived biochemical compound have been use as therapeutic drug for the treatment of many human and animal diseases. The plants extracted chemicals utilize as therapeutic medicine is called plant drug and plants secondary metabolites can also serve as drug precursors, prototypes drug, and pharmacological probes, these entire discovery by plant screening technical methods. We attempt to discuss on the Present drug discovery scenario and primitive and advanced plant drug discovery and its development and related techniques. The plant identified and screening methods to discovery of plant drug.

Natural Products are characterized by enormous scaffold diversity and structural complexity. They typically have a higher molecular mass, a larger number of sp3 carbon atoms and oxygen atoms but fewer nitrogen and halogen atoms, higher numbers of H-bond acceptors and donors, lower calculated octanol–water partition coefficients (cLogP values, indicating higher hydrophilicity) and greater molecular rigidity compared with synthetic compound libraries (Harvey Al.,*et. al.,* 2008, Fabricant DS., 2001and Smit HF*et. al.*,1995).

Over a million people in the worldwide are now confirmed to be infected with COVID- 19; we have two in India like, Covaxin and Covishields and others, empirical cure vaccines for this potentially fatal disease. Drug repurposing is playing a vital role in combination recovering of this disease. Drug repurposing or repositioning is a drug development strategy which identifies new pharmacological applications of already approved for the drugs. Drug repositioning is the discovery of new indications for approved or failed drugs. Positioning opportunities exist because drugs perturbing multiple biological entities and themselves involved in the diversified biological process. The drug discovery focused on one way of disease of interest, a therapeutic application for a drug to other areas can be abide. The therapeutic plants have an advantage in this area based on their long-time use by humans. One may expect any bioactive compounds obtained from such medicinal plant to have low human health toxicity. Obviously, these many plants may be toxic within a given of the endemic culture that has no reporting to document these effects.

The covid19 life cycle involves a number of potentially targetable step including endocytic entry into humans, host cells [Involving Angiotensin-converting Enzyme 2 (ACE2) and Transmembrane Protease Serine 2 (TMPRSS2) both of them], RNA replication and transcription [Involving Helicase and RNA-dependent RNA Polymerase (RdRP)], translation and proteolytic processing of viral proteins virion assembly, and release of new

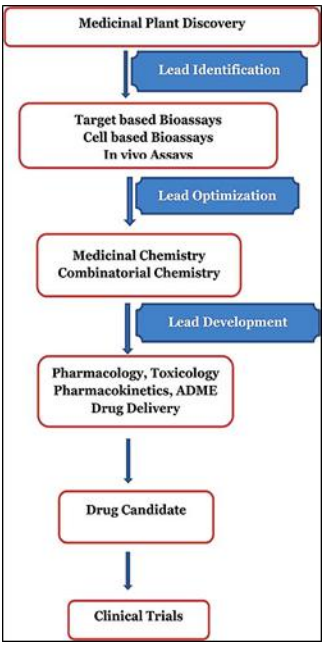
viruses through the exocytic human cell systems. In addition to virally encoded targets, numerous respiratory host targets are essential for viral replication and disease progression, like covid19 use the endolysosomal pathway to enter the cell before uncoating of the host.

1. Methods approaches through selection of candidates and species screening

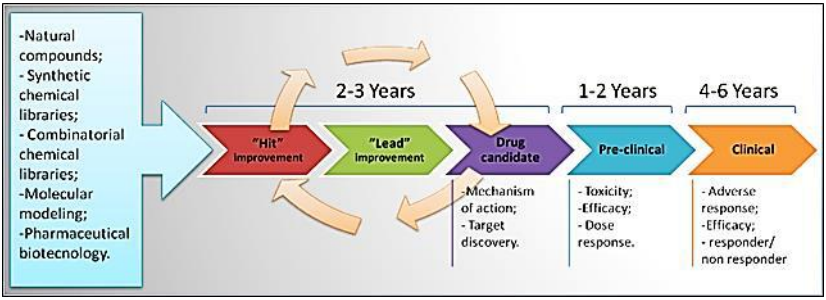
In silico is the term used to mean "performed on computer through computer simulation". In silico methods help in identifying drug targets in a less time, cheapest and cost-effective manner. The use of computers and computational methods is involvement in all aspects of drug designing, development and repurposing.

There are two major types of drug design:

1) Ligand-based drug design these is based on the knowledge of other molecules that bind to the biological target of interest. These other molecules may be used to derive a pharmacophore model that defines as the minimum necessary structural characteristics a molecule must of the possess in order to bind to target.
2) Structure-based drug design these is based on the knowledge of the three-dimensional structure of biological target obtained through methods such a x-ray crystallography and NMR spectroscopy.



There are many important methods for in-silico drug design research such as homology modelling, molecular dockin virtual high-throughput screening, quantitative structure activity relationship (QSAR) and hologram quantitative structure activity relationship (HQSAR), comparative molecular field analysis of (CoMFA), Comparative molecular similarity indices analysis (CoMSIA), 3D pharmacophore mapping, microarray analysis and conformational analysis techniques, Monte Carlo simulation and molecular dynamic (MD) simulation ((Kubiyayi, H., 1997, Cramer RD., *et. al.*,1989 &Klebe G., 1994).



A. Random approaches B. Ethnopharmacology approaches C. Traditional approaches D. Zoo-pharmacology

1) Observed out of 2.50 lakh angiosperms and gymnosperms plants species recently 6% have been screened for biological activity and about 15 percent have been screened for phytochemical activity (Fabricant DS *et al*., 2001).
2) Random approaches have been followed for screening of plants selection method through randomly for purpose of latest drug discovery. The plant screening for selected class of plants product like alkaloid flavonoidsetc.
3) Screening plants for selected bioassay, this is followed up to three decades by Central Drug Research Institute and council of scientific and industrial research of India, National Cancer Institute's (NCI), National Institutes of Health, USA.
4) The drug discovery approach of ethnopharmacology essentially depend on empirical experience related to use of plants drug for the biologically active NCEs this is through experimental, investigation, description and observation.
5) Traditional system of medicine approach in India and China has a rich heritage and well documented traditional system of medicines and plant sources.

6) Behavior of animals with a view for observation and identify the candidate's plants for view drug discovery, its observation straight tail linked to cattle grazing habit in certain habit of South America led to identification of a plant C*estrum diurinum* and three other plants members of family Solanaceae which probably are the known plant sources of the derivatives of vitamin D, this is close observation and monitoring under animal behavior (Katiyar. *Et al.*, 2015).

2. Other useable methods for the drug discovery

1) Drug chemical structure similarity.
2) Drug side- effect similarity.
3) Drug target similarity.
4) Gene ontology (GO) similarity of drug-related genes.
5) Disease phenotypic similarity.
6) Human phenotype (HPO) similarity.
7) GO similarity of disease-related genes.
8) Gold standard dataset.
9) Traditionally plants product used methods.
10) 10 Marine natural plants product isolate methods.
11) Bioinformatics methods.

3. Docking methods

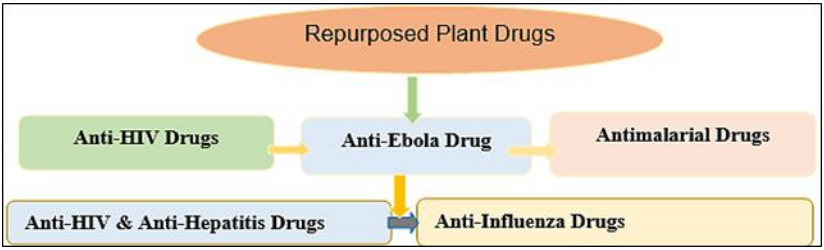
Once we chose leader compounds from the previously mentioned list, we used the COVID-19 Docking Server (https://ncov.schanglab.org.cn/), a web server that predicts the binding modes between different COVID-19 targets and the ligands. A complete description of the algorithm used for such could be found (Kong, R., *et. al.*,2020). We tested the targets: Main protease, papain-like protease, Nsp3 (AMP site), Nsp3 (MES site), RdRp (RTP site), RdRp (RNA site), Helicase (ADP site), Helicase (NCB site), Nsp14 (ExoN), Nsp14 (N7-MTase), N protein (NCB site) with the selected ligands, accordingly to the best conformation (emodin anthrone, kaempferol, quercetin, aesculin, cichoriin, luteolin, matricin, riolozatrione, monocaffeoyl tartaric acid and aucubin).

4. Pharmacokinetic assessment (PBPK Model building and evaluation)

The best compound according to docking results observe of the some reviewed against SARS-CoV-2, developed a PBPK model to predict the

pharmacokinetic potential of such compounds in an individual. In this response, the PBPK's models predict the concentration-time profile of compounds in the body, giving an idea of such compounds' to the performance. The adult PBPK model was developed using PK-sim modeling software (version 8.0, 2017, http://www. Systems biology.com/products/pk-sim.html) and according to data from simulation from other coumarins. (Miura, T., *et al.*, 2020).

A brief update on the status of potential repurposed discovery of drugs and/or combinations recently under clinical trials is following.



1) **Anti-HIV drugs:** The therapeutic, combination of lopinavir-ritonavir is used in the USA to treat HIV infections and it has selected because of its ability to inhibit protease of HIV and other SARS-CoV-2.
2) **Anti-ebola drug:** The famous drug, Remdesivir (2-ethylbutyl-L-alaninate phosphoramidate prodrug) is a novel nucleotide analogue originally developed by GILEAD Sciences to treat Ebola virus. It's used in corona viral disease treatments.
3) **Antimalarial drugs:** The beneficial effects of repurposed drug Chloroquine, Hydro-cloroquine it is anti-malarial drug used in the treatment of covid-19.
4) **Anti-influenza drugs:** Favipiravir, is a new type of RdRp inhibitor which is currently using clinical trial for the covid-19.
5) **Anti-HIV & Anti-hepatitis drugs:** The Ritonavir and Danoprevir suspension is approved for the treatment this combination with or without interferon nebulization for the treatment of COVID-19.

Caution: Above the entire drug only study purposes in this article anybody should not directly apply and practices, without permission of prescribed physician and experts. Otherwise the authors are not responsible for any effects.

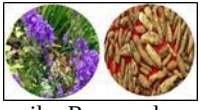
Table 3: List of potential medicine plants possessing antiviral, anti-malarial and anti-bacterial activity

S. No.	Name of the plant	Family	Important phytoconstituents	Therapeutic uses
1.	*Ocimum sanctum* (Holy Basil)	 Family: Lamiaceae	Eugenol, carvacrol, methyl eugenol, caryophyllene, linalool, cineole.	Gems, fungi and infection with anti-bacterial. The fresh mature leaves are given to children with nasal catarrh and cough, asthma, fever, constipation and worm.
2.	*Nigella sativa* (Black seed)	 Family: Ranunculaceae	Thymoquinone, Nigellimine	Influenza Virus(H9N2), Cytomegalovirus (MCMV), Hepatitis C virus, HIV
3.	*Cinchona succirubra* (Cincona)	 Family: Rubiaceae	Quinine, Quinidine, Cinchonidine, Cinchonine	Herpes simplex virus-1(HSV-1) influenza A virus (IAV)

4.	*Sambucus nigra* (Elderberry)	 Family: Caprifoliaceae	Ursolic acid, Oleanolic acid	Herpesvirus
5.	*Withania somnifera* (L.) Dunal (Ashwagandha)	 Family: Solanaceae	Withanolides, somniferinine, withaferins, Isopelletierine, anaferine, sitoinroside, anahygrine, visamine.	Herpes Simplex Virus Influenza virus H1N1
6.	*Prunella vulgaris* (Self-heal)	 Family: Lamiaceae	Betulinicacid, Hyperoside, Delphinidin, Lupeol	HIV-1 and Bola virus, Herpes Simplex Virus -1 & 2
7.	*Piper nigrum* ((Kali mirch, Maricha)	 Family: Piperaceae	Piperine, Piperdine, Piperettine, Chavicine	Used for diseases of the respiratory tract (cough, bronchitis, asthma), Increase total WBC and Bone marrow cells.

8.	*Tinospora cordifolia* (Guduchi/Giloy)	 Family: Menispermaceae	Berberin, columbin, chasmanthin, palmarin, tinosporon, tinosporic acid and tinosporol.	Used in high fever, strengthens immune system and cures various infections like cold, cough, swine flu and fever due to any reason.
9.	*Glycyrrhiza glabra* (Licorice)	 Family: Fabaceae	Glyrrhizin, Glycyrrhetic acid, Liquiritin, Isoliquiritin	HCV, Influenzavirus, HSV1
10.	*Caesalpinia pulcherrima* (Peacock flower)	 Family: Leguminoseae	Lupeol, β-amyrin, Peltoqinods, Homoisoflavonoids	Herpes viruses, adenovirus
11.	*Curcuma longa* (Turmeric)	 Family: Zingiberaceae	Curcumin, d-a-phellandrene, d-sabinene, cineol, borneol, sesquiterpenes.	HSV-1, HIV, HCV

12.	*Cinnamomum zylanicum* (dalchini, Darushila)	 Family: Lauraceae	Cinnamic aldehyde, eugenol	Plant drug as considered astringent, stimulant and carminative, check nausea; useful in gastric troubles and toothache.
13.	*Zingiber officinale* (Ginger)	 Family: Zingiberaceae	Gingerol, Shogaols, Zingerone	Avian influenza virus (H9N2)
14.	*Punica granatum* (Pomegranate)	 Family: Lythraceae	Punicalagins, Ellagitannin	SARS-Co. V -19
15.	*Andrographis paniculate* (green chireta)	 Family: Acanthaceae	Andrographolide	Antiviral properties, HSV, HBV, HCV, Chikungunya virus, HPV, HIV

16.	*Syzygium aromaticum* (Laung, lavanga)	 Family: Myrtaceae	Methyl-amyl ketone, gallotamic acid, eugenol acetate, iso-eugenol, vanillin, caryophyllin.	Antiviral properties, anti-microbial activity, powerful anti-septic, Phthisis, bronchial troubles and
17.	*Aconitum heterophyllum* (Bish, Attis)	 Family: Ranunculaceae	Biokhaconitine, indaconitine, diacetyl pseudo-aconitine.	Cardiac stimulants, arthritis, scabies.
18.	*Bacopa monnieri* (L.) (Brami, Sarasvadi)	 Family: Scrophullariaceae	Brahmine, herpastive, hersaponin, bacogenin-A, monnierin	Neuralgia, inflammation, asthma. bronchitis, syphilis, fever.
19.	*Emblica officinalis* (Amlika, Anola)	 Family: Euphorbiaceae	Emblicanin-A, Emblicanin-B,	Fruits are anti-diarrhoeal, anti-dysenteric, the are used as a collyrium in eye complaints and their infusion is given in asthma, bronchitis, and fever.

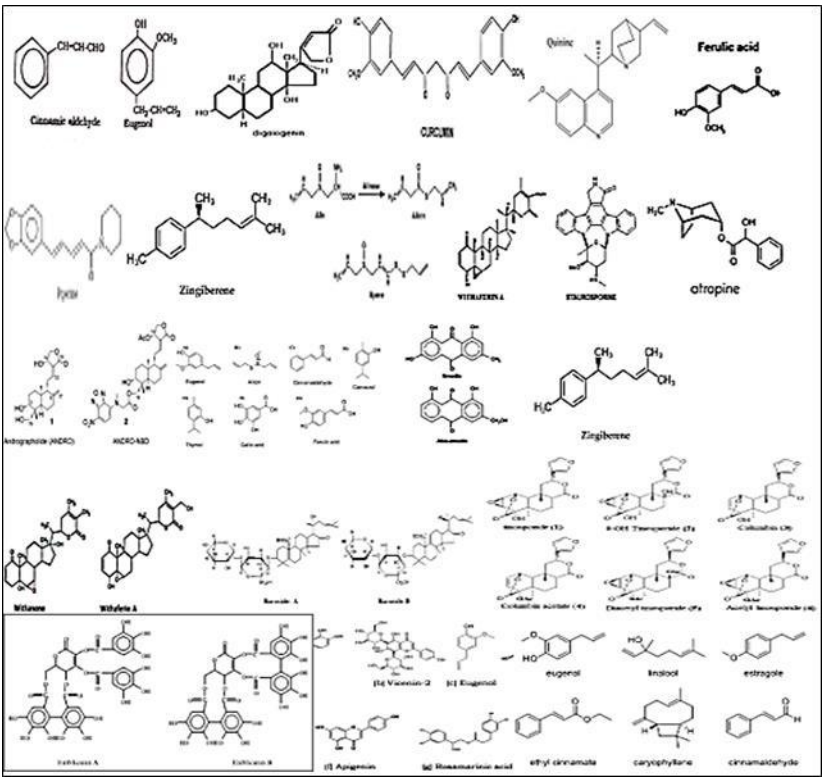


Fig 1: Chemical structure of some selected natural Products known to exhibit potent antiviral activity

They identified some of the 13 natural products, which is occur in traditional Chinese medicines and could cause antiCovid-19 activity. 125 herbs listed to contain at least two of these phytoconstituents while only 26 herbs are listed and categorically used to treat viral respiratory infections **(**Zhang DH., *et al.,* 2020). The identified chemicals include; *Quercetin, Kaempferol, Betulinic acid, Coumaryl tyramine, Cryptotanshinone, Sugiol* etc. The extra potential Chinese herbal plants containing these constituents and possibly be used to treat for respiratory syndromes are *Forsythiae fructus, Liquorice, Mori cortex, Eriobotryae folium, Ardisia japonicae herba* etc.

screened a medicinal plant database containing 32,297 potential anti-viral phytochemicals/traditional Chinese medicinal compounds and selected the top nine hits that may inhibit SARS-CoV-2 $3CL^{pro}$ activity and hence virus replication. Top ranked phytochemicals 5,7,3',4'-Tetrahydroxy2'-(3,3-dimethylallyl) isoflavone from *Psorothamnus arborescens, Myricitrin from*

Myrica cerifera, Methyl rosmarinate from Hyptisatrorubens poit, Calceolarioside B from Fraxinus sieboldiana, Licoleafol from Glycyrrhiza uralensis showed better binding affinity and docking scores than positive control drugs, Nelfinavir and Prulifloxacin. They concluded that these phytochemicals might serve as potential anti-COVID-19 lead molecules for further optimization and drug development process to combat COVID-19 **(**Qamar MT., *et. al.*,2020). On the observe several efforts have been performed to identify whether natural products possess antiviral disease effects.

This instance, aqueous extracts of *Ocimum basilicum* have been proven to be effective against enterovirus by inhibiting viral replication capacity (Chiang, LC. *Et al.,* 2005). In others observation Furthermore, saikosaponins (Cheng, PW., 2006) identified phenolic compounds, amentoflavone, myricetin and scutellarein isolated from *Lycoris radiata, Artemisia annya, Torreya nucifera* and *Lindera aggregata* are active against SARS-CoV-1 disease (Li, SY., *et al.,* 2005 &Yu, MS., Lee *et al.,* 2012).

A brief review of herbal medicine, to (Huang, J. *et al.,* 2014). Moreover, other sources of antiviral compounds have shown to possess such important properties for instance, Suwannarach *et, al.* (2020) observe that fungi are a source of natural bioactive compounds that are potentially useful for preventing viral infections and improving human immunomodulation; against disease and additionally, natural products from marine plants species have recently shown important antiviral properties (Teng, YF. *Et al.,* 2020). In the field plants therapeutic, Mexico is the fourth country with the large biodiversity globally. It has been estimated that there are more than 35,000 species of plants; and after China, Mexico is the country with the second largest number of medicinal plants (4000 spp., approximately). Moreover, Mexican ethnomedicine has a deeply rooted tradition to use herbal remedies to treat the most common health problems. In this sense, Mexican plants have been studied phytochemically, pharmacologically and anthropologically for more than 100 years, representing a significant research line in Mexico and worldwide (Mata, R., *et al.,* 2019).

Interestingly, the most frequently used plants accordingly to (Mata, R., *et, al.*,2019 & Valdivia-Correa *et. al.*,2016)are *Opuntia Ficus, Scoparia dulcis, Citrus aurantium, Prunus persica, Rosmarinus officinalis, Prunus persica, Rosmarinus officinalis, Equisetum hyemale, Tiliamexicana, Mentha piperita, Larrea divaricata, Taraxacum officinale, Morus alba, Verbascum densiflorum, Matricariarecutita, Urtica dioica, Passiflora incarmata, Tiliaeuropea* and *Aloa Vera* most of which have shown several

pharmacological properties such as antiparasitic, pain and menstrual pain relief, issues of the nervous system, among others.

Conclusion

In Ayurveda 2000 plants species are considered to have medicinal values while Chinese's pharmacopoeia listed over 5700 traditional plants medicines. Indian medicinal plant has a good contribution to the development of *material medica*. The Charak Samhita is one of the earliest treatises in Indian medicines it was recorded the use of over 340 vegetable drugs. In European, Asian, Australian, American countries have a great plant medicine produce system and they develop latest drug discovery institutions. *Liquorice, Zinger Turmeric, Green Chireyta, Winter Cherry* are widely used Indian system of medicines for upper respiratory infection since ancient time. To the traditional plant therapeutic medicines system be implement in future because our native traditional therapeutic plant medicines very effective and cheapest available locally. India is greatest and largest country in the context of biodiversity plant diversity and natural resources, in India nearabout, absolutely important plant species found in naturally grown condition we have much and more resources in compare to other develop and developing countries of the world, our scientist, technologist, do great effort to implementation of technologies for this. Covid-19 is worldwide pandemic disease caused by novel corona viruses, SARS-CoV-2 these is effects humans' respiratory system. In the world nearabout 10 million people causing death up-to April 2021, and worldwide crisis for the socio-economy. These is one of the challenges to treatment of pharmacological and therapeutic plant medicines for this we should development our natural and plant resource and our technology to the issue of forthcoming self-dependent and implemented our techno friendly policy. *Glycyrrhizin* and *Glycyrrhetinic* acid the bioactive constituents of licorice (*Glycyrrhiza glabra*) can induce nitrous oxide synthetase which in turn blocks viral replication.

Various authors give good idea through the review about recent disease susceptibility and their therapeutic drug discovery through the plants. CADD- Computer-added drug design, RDD-Rational drug design, CAMD-Computer assisted molecular modelling, SBDD-Structure Based Drug Design MTDs-Multi Target Drugs, QSAR-Quantitative Structure Activity Relationship LBDD-Ligand based Drug Design. Another example is that deep learning methods will become a major computer, added drug design discovery approach in the near future. A new paradigm in drug discovery of the poly pharmacology, which is the process off in ding new uses for existing approached drug which focuses on multi targets drugs (MTDs). To

drug design approach many novel technologies and methodologies will be develop to implement the drug discovery process and should effort drug discovery related program those dependent on computational methodologies these are future prediction and checked experimental results. Many advances discussed above are supported by computational tools including data bases such as genomic chemical spectral analysis data for a recent review on natural product tools that enable the analysis of genetic information the prediction of chemical structures and pharmacological activities.

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