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MEDICINAL PLANTS - THE BASE OF HOLISTIC MEDICINE IN UNIVERSE

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ABSTRACT

Nature provides so many holistic units from flora and fauna which are essential for diagnosis and cure of diseases produced by pathogenic and non-pathogenic sources. So many herbal sources produce numbers of macromolecules as well as micronutrients which are essential for body. These are produced from organized and unorganized sources of herbal units eg. Alkaloids, Glycosides, Tannins, Carbohydrates, Proteins, Lipids, Vitamins, Minerals, Enzymes etc, by biosynthesis followed by biogenesis. Medicinal plants produce drugs which are biologically active to combat over the malfunction of normal body system because all drugs are xenobiotics which come from outer source and goes inside the living body to control over the biochemical and physicochemical parameters.

KEYWORDS: Anti-Cancerous Drug, Anti-Malarial Drug, Anti-Hypertensive Drug, Vinblastine, Vincristine, Quinine, Reserpine

INTRODUCTION

The earliest historical records of herbs are found from the Sumerian Civilization, where hundreds of medicinal plants including opium are listed on clay tablets. The Ebers Papyrus from ancient Egypt, c. 1550 BC, describes over 850 plant medicines. The Greek physician Dioscorides, who worked in the Roman army, documented over 1000 recipes for medicines using over 600 medicinal plants in De materia medica, c.60 AD; this formed the basis of pharmacopoeias for some 1500 years. Drug research makes use of ethno-botany to search for pharmacologically active substances in nature, and has in this way discovered hundreds of useful compounds. Medicinal plants are widely used in non-industrialized societies, mainly because they are readily available and cheaper than modern medicines.[1]

VINCA

Vinca is a genus of flowering plants in the family Apocynaceae, native to Europe, northwest Africa and southwest Asia. The English name **periwinkle** is shared with the related genus *Catharanthus* (and also with the common seashore mollusc, *Littorina littorea*).[2]

1. *Vinca difformis* Pourr. – Azores, western and central Mediterranean
2. *Vinca erecta* Regel & Schmalh. – Afghanistan, Kyrgyzstan, Tajikistan, Uzbekistan
3. *Vinca herbacea* Waldst. & Kit. – central, eastern and South-Eastern Europe; Middle East
4. *Vinca major* L. – southern Europe, Turkey, Syria, Caucasus; introduced to and established in New Zealand, California, British Isles, central Europe, Ukraine, North Africa, south China, Canary Islands, Madeira, North America, Mexico, Colombia, Venezuela, Peru, Costa Rica, Guatemala
5. *Vinca minor* L. – central and southeastern Europe, Ukraine, Caucasus; introduced to and established in British Isles, Scandinavia, Portugal, Turkey, south China, North America, New Zealand
6. *Vinca soneri* Koyuncu – Turkey
7.

Figure 1: Vinca plant

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VINCA (Scientific classification)

Kingdom:	Plantae
Clade:	Tracheophytes
Clade:	Angiosperms
Clade:	*Eudicots*
Clade	Asterids
Order:	Gentianales
Family:	Apocvnaceae
Subfamily:	Rauvolfioideae
Tribe:	Vinceae
Subtribe:	Vinceae M.E.Endress
Genus:	Vinca L. 1753

Medicinal Use

The vinca alkaloids include at least 86 alkaloids extracted from plants in the genus *Vinca*. The chemotherapy agent **vincristine** is extracted from a closely related species, ***Catharanthus roseus***, and is used to treat some leukemias, lymphomas, and childhood cancers, as well as several other types of cancer and some non-cancerous conditions. **Vinblastine** is a chemical analogue of **vincristine** and is also used to treat various forms of cancer. Dimeric alkaloids such as **vincristine** and **vinblastine** are produced by the coupling the smaller indole alkaloids **vindoline** and **catharanthine**.

In addition, the nootropic agent vincamine is derived from ***Vinca minor***. **Vinorelbine**, a newer semi-synthetic chemotherapeutic agent, is used in the treatment of non-small-cell lung cancer and is prepared either from the natural products **leurosine** or **catharanthine** and **vindoline** in both cases by first preparing **anhydrovinblastine**.[3]

Vinblastine (**VBL**), sold under the brand name **Velban** among others, is a chemotherapy medication typically used with other medications, to treat a number of types of cancer. This includes Hodgkin's Lymphoma non-small cell lung cancer, bladder cancer, brain cancer, melanoma, and testicular cancer. It is given by injection into a vein.[4]

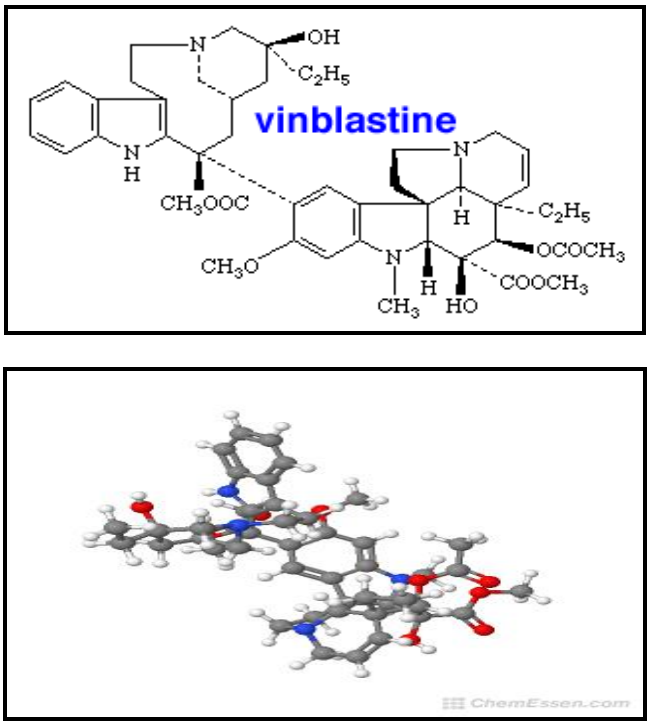


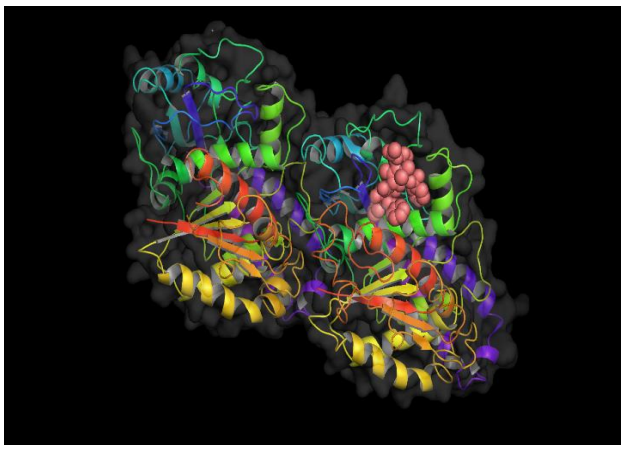
Figure 2: Normal & 3D Structure of Vinblastine

Vinblastine is a component of a number of chemotherapy regimens, including ABVD for Hodgkin lymphoma. It is also used to treat histiocytosis according to the established protocols of the Histiocytosis Association.

Vinblastine is a vinca alkaloid and a chemical analogue of vincristine. It binds tubulin thereby inhibiting the assembly of microtubules Vinblastine treatment causes M phase specific cell cycle arrest by disrupting microtubule assembly and proper formation of the mitotic spindle and the kinetochore each of which are necessary for the separation of chromosomes during anaphase of mitosis. Toxicities include bone marrow suppression (which is dose-limiting), gastrointestinal toxicity, potent vesicant (blister-forming) activity, and extravasation injury (forms deep ulcers). Vinblastine paracrystals may be composed of tightly-packed unpolymerized tubulin or microtubules.[5]

Mechanism of Action

Microtubule disruptive drugs like vinblastine, colcemid and nocodazole have been reported to act by two mechanisms. At very low concentrations they suppress microtubule dynamics and at higher concentrations they reduce microtubule polymer mass. Recent findings indicate that they also produce microtubule fragments by stimulating microtubule minus-end detachment from their organizing centers. Dose-response studies further indicate that enhanced microtubule detachment from spindle poles correlate best with cytotoxicity.



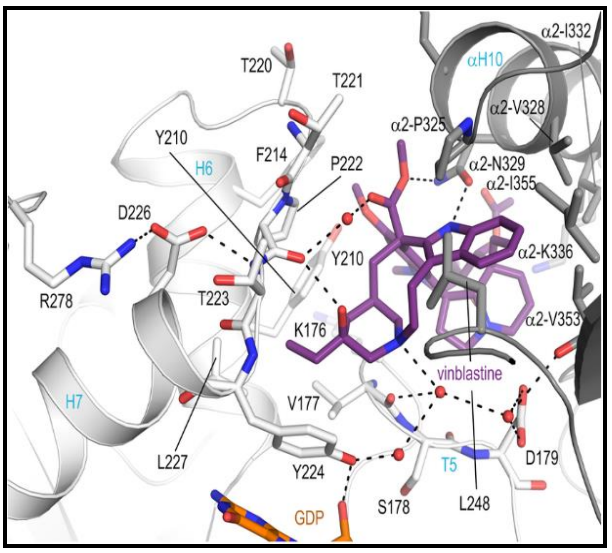


Figure 3: Tubulin and Vinblastine Complex Vinblastine is showed yellow coloured here

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Isolation and biosynthesis

Vinblastine may be isolated from the Madagascar Periwinkle (***Catharanthus roseous***) along with several of its precursors, catharanthine and vindoline. Extraction is costly and yields of vinblastine and its precursors are low, although procedures for rapid isolation with improved yields avoiding auto-oxidation have been developed. Enantioselective synthesis has been of considerable interest in recent years, as the natural mixture of isomers is not an economical source for the required C16′S, C14′R stereochemistry of biologically active vinblastine. Initially, the approach depends upon an enantioselective Sharpless epoxidation, which sets the stereochemistry at C20. The desired configuration around C16 and C14 can then be fixed during the ensuing steps. In this pathway, vinblastine is constructed by a series of cyclization and coupling reactions which create the required stereochemistry. The overall yield may be as great as 22%, which makes this synthetic approach more attractive than extraction from natural sources, whose overall yield is about 10%. Stereochemistry is controlled through a mixture of chiral agents (Sharpless catalysts), and reaction conditions (temperature, and selected enantiopure starting materials).[6]

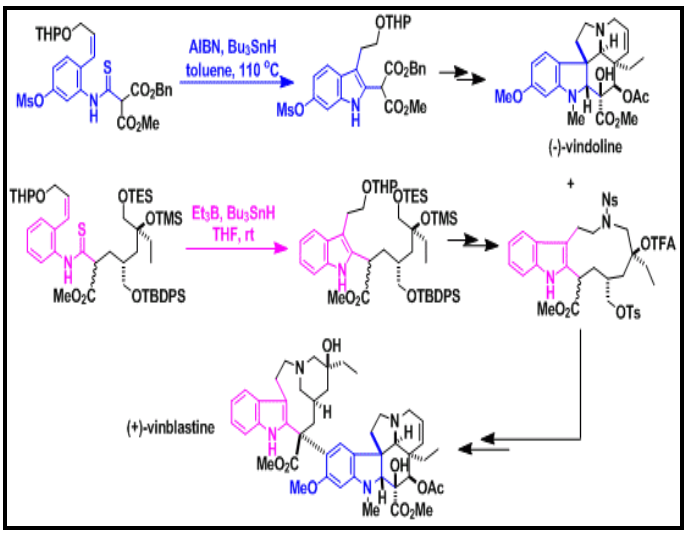
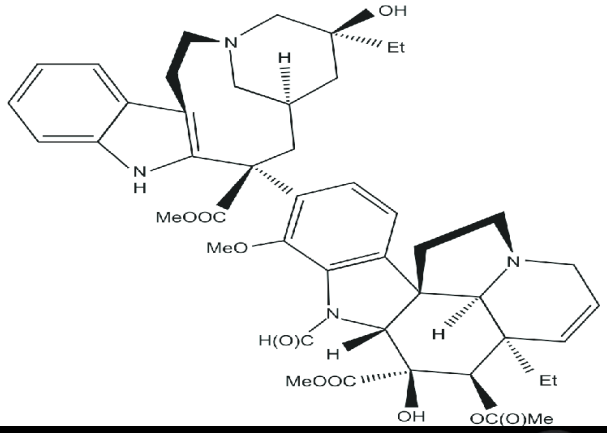


Figure 4: Biosynthesis of vinca alkaloids[5]

Vincristine, also known as **leurocristine** and marketed under the brand name **Oncovin** among others, is a chemotherapy medication used to treat a number of types of cancer. This includes acute lymphatic leukemia, acute myeloid leukemia, Hodgkin's Disease, Neuroblastoma and small cell lung cancer among others. It is given intravenously.

Mechanism of Action

Vincristine works partly by binding to the tubulin protein, stopping the tubulin dimers from polymerizing to form microtubules, causing the cell to be unable to separate its chromosomes during the metaphase. The cell then undergoes apoptosis. The vincristine molecule inhibits leukocyte production and maturation. A downside, however, to Vincristine is that it does not only affect the division of cancer cells. It affects all rapidly dividing cell types, making it necessary for the very specific administration of the drug. [7]



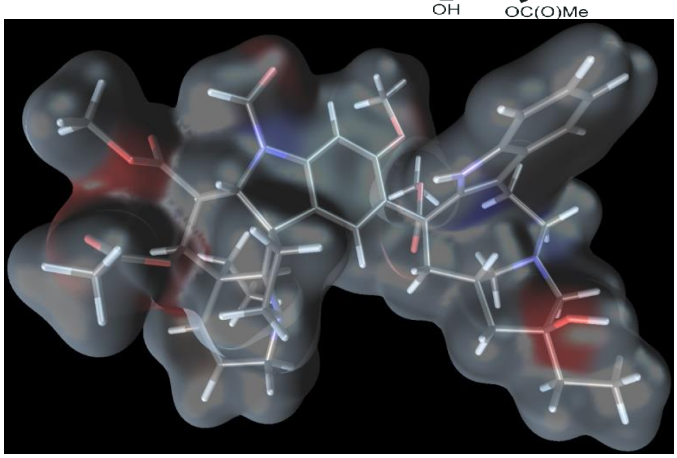


Figure 5: Normal & 3D Structure of Vincristine

The natural extraction of vincristine from ***Catharanthus roseus*** is produced at a percent yield of less than 0.0003%. For this reason, alternate methods to produce synthetic vincristine are being used. Vincristine is created through the semi-synthesis coupling of indole alkaloids vindoline and catharanthine in the vinca plant. It can also now be synthesized through a total synthesis technique which retains the correct stereochemistry at C18' and C2'. The absolute stereochemistry at these carbons is responsible for vincristine's anticancer activity.

The liposome encapsulation of vincristine enhances the efficacy of the vincristine drug while simultaneously decreasing the neurotoxicity associated with it. Liposome encapsulation increases vincristine's plasma concentration and circulation lifetime in the body, and allows the drug to enter cells more easily.

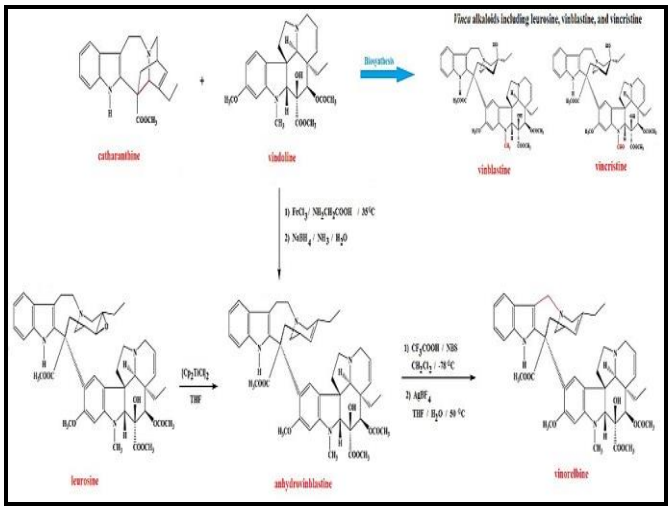


Figure 6: Biosynthesis of indole alkaloids[7]

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CINCHONA

Cinchona (pronounced /sɪŋˈkoʊnə/ or /sɪnˈtʃoʊnə/) is a genus of flowering plants in the family Rubiaceae containing at least 23 species of trees and shrubs. All are native to the tropical Andean forests of western South America.

A few species are reportedly naturalized in Central America, Jamaica, French Polynesia, Sulawesi, Saint Helena in the South Atlantic, and São Tomé and Príncipe off the coast of tropical Africa, and others have been cultivated in India and Java, where they have formed hybrids.[8]

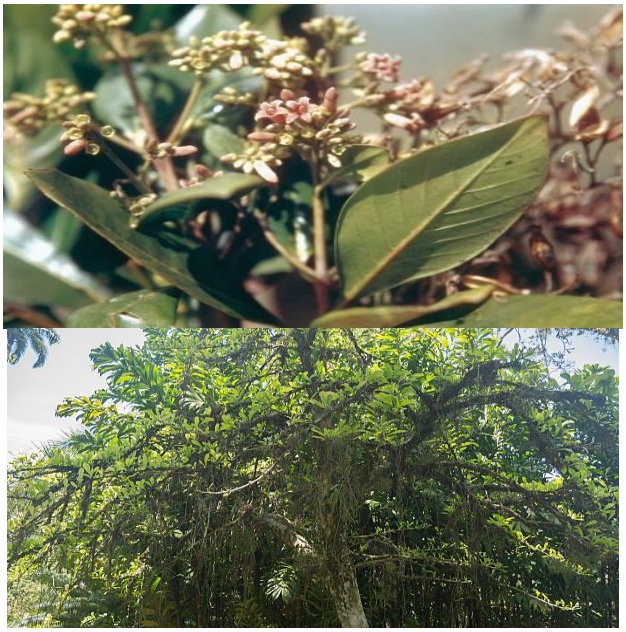

Figure 7: Cinchona plant *Cinchona pubescens* – flowers and tree

Scientific classification

Kingdom:	Plantae
Clade:	Tracheophyte
Clade:	Angiosperms
Clade:	Eudicots
Clade:	Asterids
Order:	Gentianales
Family:	Rubiaceae
Subfamily:	Cinchonoideae
Tribe:	Cinchoneae
Genus:	*Cinchona L.*

Species *Cinchona officinalis*

Description

Cinchona plants belong to the family Rubiaceae and are large shrubs or small trees with evergreen foliage, growing 5 to 15 m (16 to 49 ft) in height. The leaves are opposite, rounded to lanceolate, and 10–40 cm long. The flowers are white, pink, or red, and produced in terminal panicles. The fruit is a small capsule containing numerous seeds. A key character of the genus is that the flowers have marginally hairy corolla lobes. The tribe Cinchoneae includes the genera *Cinchonopsis*, *Jossia*, *Ladenbergia*, *Remijia*, *Stilpnophyllum*, and *Ciliosemina*. In South America, natural populations of *Cinchona* species have geographically distinct distributions. During the 19th century, the introduction of several species into cultivation in the same areas of India and Java, by the English and Dutch East India Company, respectively, led to the formation of hybrids.

Carl Linnaeus described the genus based on the species *Cinchona officinalis*, which is found only in a small region of Ecuador and is of little medicinal significance. Nearly 300 species were later described and named in the genus, but a revision of the genus in 1998 identified only 23 distinct species.[9]

Scientific identification

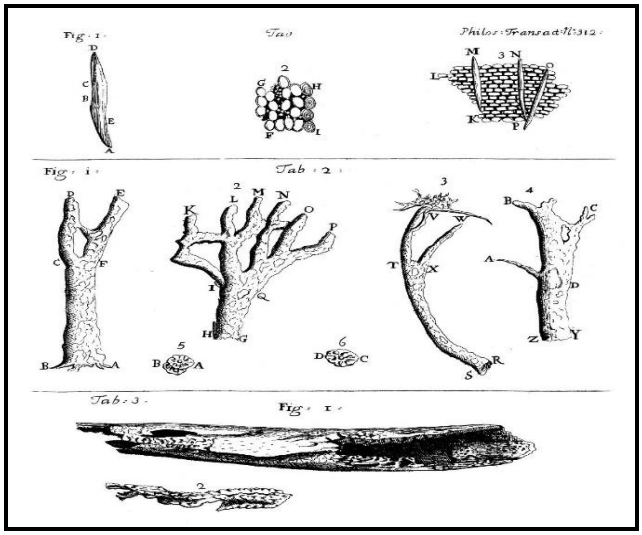

Figure 8: *Cortex peruvianus* study by Antonie van Leeuwenhoek, 1706 [2].

The "fever tree" was finally described carefully by the astronomer Charles Marie de la Condamine, who visited Quito in 1735 on a quest to measure an arc of the meridian. The species he described, *Cinchona officinalis*, was, however, found to be of little therapeutic value. The first living plants seen in Europe were *C. calisaya* plants grown at the *Jardin des Plantes* from seeds collected by Hugh Algernon Weddell from Bolivia in 1846.

The English explorer Clements Markham went to collect plants that were introduced in Sri Lanka and the Nilgiris of southern India in 1860. The main species introduced were *Cinchona succirubra*, or red bark, as its sap turned red on contact with air, and *Cinchona calisaya*. The alkaloids quinine and cinchonine were extracted by Pierre Joseph Pelletier and Joseph Bienaimé Caventou in 1820. Two more key alkaloids, quinidine and cinchonidine, were later identified and it became a routine in quinology to examine the contents of these components in assays. The yields of quinine in the cultivated trees were low and it took a while to develop sustainable methods to extract bark.

Francesco Torti used the response of fevers to treatment with cinchona as a system of classification of fevers or a means for diagnosis. The use of cinchona in the effective treatment of malaria brought an end to treatment by bloodletting and long-held ideas of humorism from Galen. For his part in obtaining and helping the establishment of cinchona in British India, Clements Markham was knighted. For his role in establishing cinchona in Indonesia, Hasskarl was knighted with the Dutch order of the Lion.

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Traditional medicine

In herbalism, cinchona bark was used as an adulterant in Jesuit's bark or Peruvian bark which originally is thought to have referred to ***Myroxylon peruiferum***, another fever remedy. The bark of cinchona can be harvested in a number of ways. One approach was to cut the tree but this and girdling are equally destructive and unsustainable so small strips were cut and various techniques such as "mossing", the application of moss to the cut areas, were used to allow the tree to heal. Other approaches involved coppicing and chopping of side branches which were then stripped of bark. The bark was dried into what were called quills and then powdered for medicinal uses. The bark contains alkaloids, including quinine and quinidine. Cinchona is the only economically practical source of quinine, a drug that is still recommended for the treatment of *falciparum* malaria.[10]

Homeopathy

The birth of homeopathy was based on cinchona bark testing. The founder of homeopathy, Samuel Hahnemann, when translating William Cullen's *Materia medica*, noticed Cullen had written that Peruvian bark was known to cure intermittent fevers. Hahnemann took daily a large, rather than homeopathic, dose of Peruvian bark. After two weeks, he said he felt malaria-like symptoms. This idea of "like cures like" was the starting point of his writings on homeopathy. Hahnemann's symptoms have been suggested by researchers, in homeopathy as being an indicator of his hypersensitivity to quinine.

Cinchona alkaloids

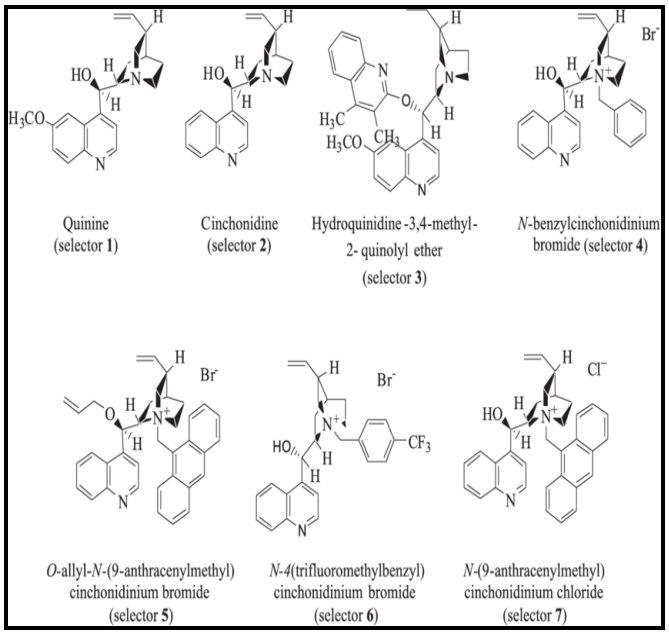

Figure 9: General structure of *Cinchona* alkaloids[11]

The bark of trees in this genus is the source of a variety of alkaloids, the most familiar of which is quinine, an antipyretic (antifever) agent especially useful in treating malaria. For a while the extraction of a mixture of alkaloids from the cinchona bark, known in India as the cinchona febrifuge, was used. The alkaloid mixture or its sulphated form mixed in alcohol and sold quinetum was however very bitter and caused nausea, among other side effects.

Cinchona alkaloids include:

They find use in organic chemistry as organocatalysts in asymmetric synthesis.

Alongside the alkaloids, many cinchona barks contain cinchotannic acid, a particular tannin, which by oxidation rapidly yields a dark-coloured phlobaphene called red cinchonic, cinchono-fulvic acid, or cinchona red.[11]

Figure 10: Bark of Cinchona

In 1934, efforts to make malaria drugs cheap and effective for use across countries led to the development of a standard called "totaquina" proposed by the Malaria Commission of the League of Nations. Totaquina required a minimum of 70% crystallizable alkaloids, of which at least 15% was to be quinine with not more than 20% amorphous alkaloids.

Quinine is an antimalerial drug

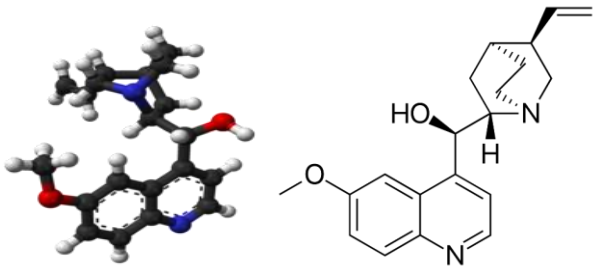

Figure 11: Quinine 3D & normal structure

Quinine is a medication used to treat malaria and babesiosis. This includes the treatment of malaria due to *Plasmodium falciparum* that is resistant to chloroquine when artesunate is not available. While used for restless legs syndrome it is not recommended for this purpose due to the risk of side effects. It can be taken by mouth or used intravenously. Malaria resistance to quinine occurs in certain areas of the world. Quinine is also the ingredient in tonic water that gives it its bitter taste.[12]

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Common side effects include headache, ringing in the ears, trouble seeing, and sweating. More severe side effects include deafness, low blood platelets, and an irregular heartbeat. Use can make one more prone to sunburn. While it is unclear if use during pregnancy causes harm to the baby, use to treat malaria during pregnancy is still recommended. Quinine is an alkaloid a naturally occurring chemical compound. How it works as a medicine is not entirely clear.

Quinine was first isolated in 1820 from the bark of a cinchona tree. Bark extracts have been used to treat malaria since at least 1632. It is on the World Health Organisation's List Of Essential Medicines the safest and most effective medicines needed in a health system.

Available forms

Quinine is a basic amine and is usually provided as a salt. Various existing preparations include the hydrochloride, dihydrochloride, sulfate, bisulfate and gluconate.

All quinine salts may be given orally or intravenously (IV); quinine gluconate may also be given intramuscularly (IM) or rectally (PR). The main problem with the rectal route is that the dose can be expelled before it is completely absorbed; in practice, this is corrected by giving a further half dose.[13]

Name	Quinine base equivalence
Quinine base	100 mg
Quinine bisulfate	169 mg
Quinine dihydrochloride	122 mg
Quinine gluconate	160 mg
Quinine hydrochloride	111 mg
Quinine sulfate dihydrate [(quinine)$_2$ H_2SO_4·2H_2O]	121 mg

Figure 12: Fluorescence from quinine[13]

Tonic Water in normal light and ultraviolet "black light" The quinine content of tonic water causes it to fluoresce under black light. Quinine is a flavor component of tonic water and bitter lemon drink mixers.

According to tradition, the bitter taste of anti- malarial quinine tonic led British colonials in India to mix it with qin, thus creating the qin and tonic cocktail, which is still popular today. Nowadays, the amount of quinine in tonic is much lower and drinking it against malaria is ineffective. In the US, quinine is listed as an ingredient in some Diet Snapple flavors, including Cranberry-Raspberry.

Mechanism of Action

Quinine is theorized to be toxic to the malarial pathogen, ***Plasmodium falciperum*** by interfering with the parasite's ability to dissolve and metabolize hemoglobin. As with other quinoline antimalarial drugs, the mechanism of action of quinine has not been fully resolved.] The most widely accepted hypothesis of its action is based on the well-studied and closely related quinoline drug, chloroquine. This model involves the inhibition of hemozoin biocrystalization in Heme Detoxification pathway, which facilitates the aggregation of cytotoxic heme. Free cytotoxic heme accumulates in the parasites, causing their deaths. Quinine may target malaria's purine neucleoside phosphorilase enzyme.[14]

Synthesis

Cinchona trees remain the only economically practical source of quinine. However, under wartime pressure, research towards its synthetic production was undertaken. A formal chemical synthesis was accomplished in 1944 by American chemists R.B. Woodward and W.E.Doering. Since then, several more efficient quinine total syntheses have been achieved, but none of them can compete in economic terms with isolation of the alkaloid from natural sources. The first synthetic organic dye, mauveine was discovered by William Henry Perkin in 1856 while he was attempting to synthesize quinine.[15]

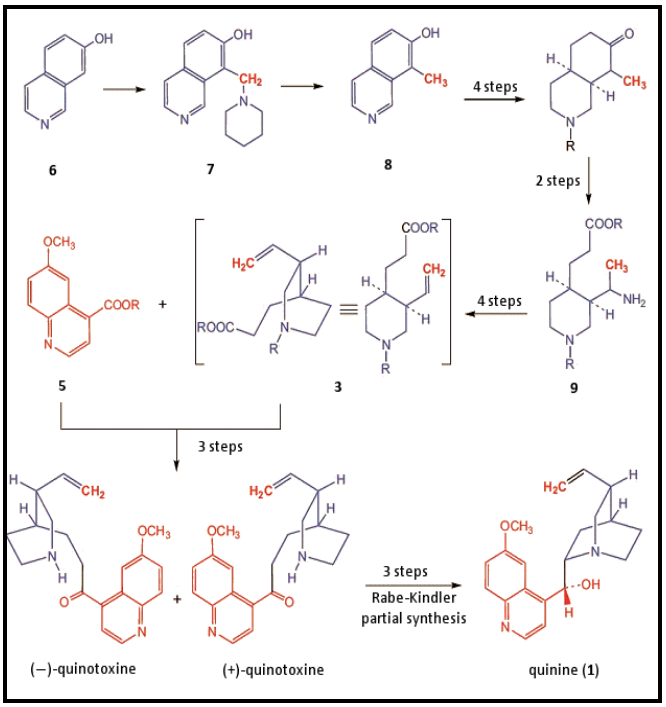

Figure 13: Biosynthesis of quinine[14]

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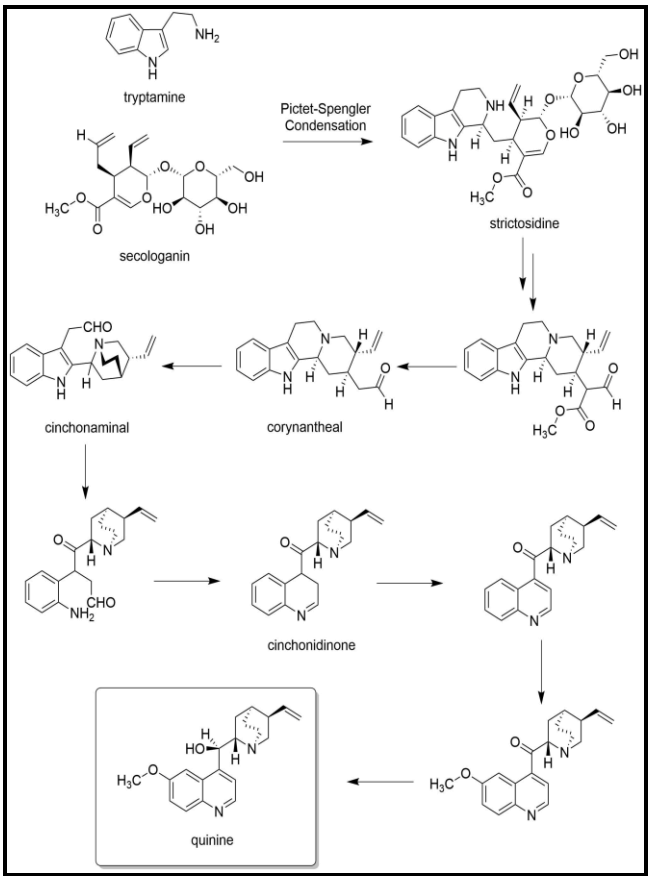

Figure 14: Biosynthesis of quinine alkaloids[15]

In the first step of quinine biosynthesis, the enzyme strictosidine synthase catalyzes a stereoselective Pictet-Spengler Reaction between tryptamine and secologanin to yield Suitable modification of strictosidine leads to an aldehyde. Hydrolysis and decarboxylation would initially remove one carbon from the iridoid portion and produce corynantheal. Then the tryptamine side-chain are cleaved adjacent to the nitrogen, and this nitrogen was then bonded to the acetaldehyde function to yield cinchonaminal. Ring opening in the indole heterocyclic ring could generate new amine and keto functions. The new quinoline heterocycle would then be formed by combining this amine with the aldehyde produced in the tryptamine side-chain cleavage, giving cinchonidinone. For the last step, hydroxylation and methylation gives quinine.

RAUVOLFIA SERPENTINA

Figure 15: Rauvolfia plant

Rauvolfia serpentina, the Indian snakeroot, devil pepper, or serpentine wood, is a species of flower in the milkweed family Apocynaceae. It is native to the Indian subcontinent and East Asia (from India to Indonesia). Rauvolfia is a perennial undershrub widely distributed in India in the sub-Himalayan regions up to 1,000 metres (3,300 ft.).[16]

Scientific Classification

Kingdom:	*Plantae*
Clade:	***Tracheophytes***
Clade:	***Angiosperms***
Clade:	***Eudicots***
Clade:	***Asterids***
Order:	***Gentianales***
Family:	***Apocynaceae***
Genus	***Rauvolfia***
Species:	***R. serpentine***

Synonyms:-
Ophioxylon album
Ophioxylon obversum
Ophioxylon salutiferum
Ophioxylon serpentinum
Ophioxylon trifoliatum
Rauvolfia obversa
Rauvolfia trifoliata

Chemical composition:-
Rauvolfia serpentina contains dozens of alkaloids of the indole alkaloid family, including ajmaline, ajmalicine, reserpine, and serpentine, among others.

Potential therapeutic effects:-
Rauwolfia serpentina is the source of the **phytochemical, reserpine**, which has been used in the treatment of systolic hypertension, although its dose-response effects remained uncertain from limited clinical research, as of 2016.

Potential adverse effects:-
Rauvolfia serpentina may cause adverse effects by interacting with various prescription drugs or via interference with mechanisms of **mental depression** or **peptic ulcer**. The reserpine in ***R. serpentina*** is associated with diverse adverse effects, including vomiting, diarrhoea, dizziness, headache, anxiety, or hypersensitivity reactions.
Potential Drug extracted: - ***Reserpine.***
Reserpine is a drug that is used for the treatment of high blood pressure, usually in combination with a thiazide diuretic or vasodilator. Large clinical trials have shown that combined treatment with reserpine plus a thiazide diuretic reduces mortality of people with hypertension. Although the use of reserpine as a solo drug has declined since it was first approved by the FDA in 1955, a review recommends use of reserpine and a thiazide diuretic or vasodilator in patients who do not achieve adequate lowering of blood pressure with first-line drug treatment alone. The reserpine-hydrochlorothiazide combo pill was the 17th most commonly prescribed of the 43 combination antihypertensive pills available in 2012. The antihypertensive actions of reserpine are largely due to its antinoradrenergic effects, which are a result of its ability to deplete catecholamines (among other monoamine neurotransmitters) from peripheral sympathetic nerve

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endings. These substances are normally involved in controlling heart rate, force of cardiac contraction and peripheral vascular resistance. At doses of 0.05 to 0.2 mg per day, reserpine is well tolerated; the most common adverse effect being nasal stuffiness.

Reserpine has also been used for relief of psychotic symptoms. A review found that in persons with schizophrenia, reserpine and chlorpromazine had similar rates of adverse effects, but that reserpine was less effective than chlorpromazine for improving a person's global state.[17]

Pharmacokinetic data:

Bioavailability	50%
Metabolism	gut/liver
Elimination half-life	Phase 1 = 4.5h,/ Phase 2 = 271h
Average	33h
Excretion	62% feces / 8% urine

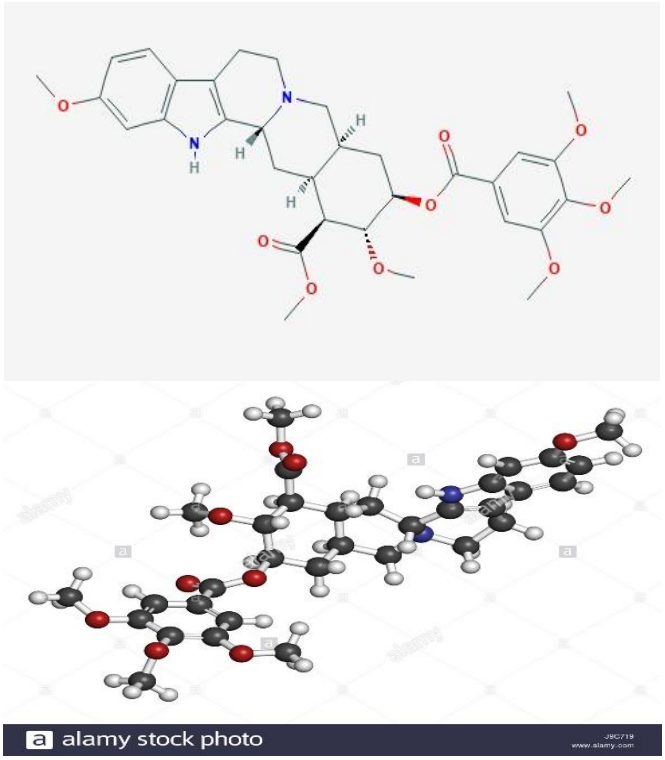

Figure 16: Normal & 3D Structure of Reserpine[16]

Mechanism of action:

Reserpine irreversibly blocks the H+-coupled vesicular monoamine transporters, VMAT1 and VMAT2. VMAT1 is mostly expressed in neuroendocrine cells. VMAT2 is mostly expressed in neurons. Thus, it is the blockade of neuronal VMAT2 by reserpine that inhibits uptake and reduces stores of the monoamine neurotransmitters norepinephrine, dopamine, serotonin and histamine in the synaptic vesicles of neurons. VMAT2 normally transports free intracellular norepinephrine, serotonin, and dopamine in the presynaptic nerve terminal into presynaptic vesicles for subsequent release into the synaptic cleft ("exocytosis"). Unprotected neurotransmitters are metabolized by MAO (as well as by COMT), attached to the outer membrane of the mitochondria in the cytosol of the axon terminals, and consequently never excite the post-synaptic cell. Thus, reserpine increases removal of monoamine neurotransmitters from neurons, decreasing the size of the neurotransmitter pools, and thereby decreasing the amplitude of neurotransmitter release. It may take the body days to weeks to replenish the depleted VMATs, so reserpine's effects are long-lasting.

Biosynthetic pathway:

Reserpine is one of dozens of indole alkaloids isolated from the plant ***Rauvolfia serpentina***. In the Rauvolfia plant, tryptophan is the starting material in the biosynthetic pathway of reserpine, and is converted to tryptamine by tryptophan decarboxylase enzyme. Tryptamine is combined with secologanin in the presence of strictosidine synthetase enzyme and yields strictosidine. Various enzymatic conversion reactions lead to the synthesis of reserpine from strictosidine.[18]

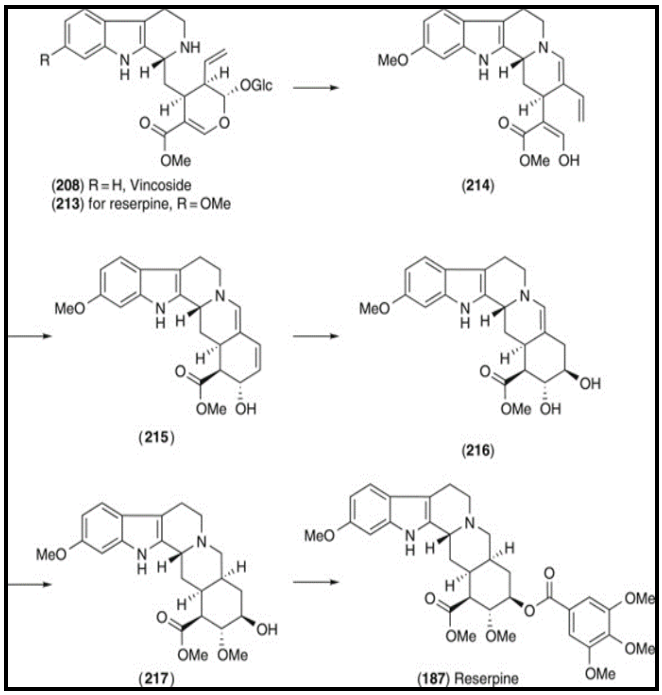

Figure 17: Biosynthesis of reserpine[17]

CONCLUSION:

God has created this earth and earth has been converted into world with various flora and fauna. Drugs from natural source coming as xenobiotic (xenus=outer source + bioticon=active in biological system) from plants as flora, from fauna as animals. Some drugs are also available from minerals source. These natural drugs are classified into two sections: organised drug and unorganised drugs. Organised drugs are obtained from parts of flora (root, stem, bark, leaf, flower, fruit, seed etc) which has definite shape and structure and Unorganised drugs are obtained as latex, gum, exudate etc which does not have definite shape and structure. Both organised and unorganised drugs from natural source have definite structural entity have binding capacity with the macromolecular receptor molecule to show drug action *in-vivo*. Every natural drugs are the category of alkaloids, glycosides, terpenes, sterols,

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phospholipids etc class which are biosynthesised inside the cell of plant via enzymatic steps *in-vivo* of plant cell by biogenesis steps originated from micronutrients of single entities like carbohydrate, amino acids, fatty acids the three main units to produce big moieties of natural products like quinine, reserpine, ergosterol, saponins etc made by carbon, hydrogen, oxygen, nitrogen, sulfur the essential elements present in the periodic table of Mendeleev. The creativity of almighty God in natural science is so meticulously followed that this *in-vivo* steps of biosynthesis in plant cell is done *in-vitro* steps in laboratory synthetic process to get the plant products large scale by structure elucidation by following the reaction steps followed by various name reactions of heterocyclic synthesis. Natural products extraction gives the products but in very less scale because the cellular contents of these holistic drugs are present in minute scale but active in large scale in body.

REFERENCE:

[1] Deborah Kopka (2011). Central & South America. Milliken Pub. Co. p. 130.
[2] Andersson, Lennart; Antonelli, Alexandre (2005). "Phylogeny of the tribe Cinchoneae (Rubiaceae), its position in Cinchonoideae, and description of a new genus, Ciliosemina". Taxon. 54 (1): 17–28.
[3] Andersson, Lennart (1998). "A revision of the genus Cinchona (Rubiaceae-Cinchoneae)". Memoirs of the New York Botanical Garden. 80: 1–75.
[4] Linné, Carolus von. Genera Plantarum 2nd edition 1743. page 413.
[5] Crawford, Matthew James (2014). "An Empire's Extract: Chemical Manipulations of Cinchona Bark in the Eighteenth-Century Spanish Atlantic World". Osiris. 29 (1): 215–229.
[6] Meyer, Christian G.; Marks, Florian; May, Jürgen (2004). "Editorial: Gin tonic revisited". Tropical Medicine & International Health. 9 (12): 1239–1240.
[7] Crespo, Fernando I. Ortiz (1995). "Fragoso, Monardes and pre-Chinchonian knowledge of Cinchona". Archives of Natural History. 22 (2): 169–181.
[8] Bergman, George J (1948). "The history and importance of cinchona bark as an anti-malarial febrifuge". Science Education. 32 (2): 93–103.
[9]Haggis, A.W. (1941). "Fundamental errors in the early history of Cinchona". Bulletin of the History of Medicine. 10 (3–4): 417–459, 568–592.
[10] King, George (1880). A manual of Cinchona cultivation in India (2 ed.). Calcutta: Government Press. pp. 1–2.
[11] Kirkbride, Jr., Joseph H. (1982). "The Cinchona Species of Jose Celestino Mutis". Taxon. 31 (4): 693–697. doi:10.2307/1219686. JSTOR 219686.
[12] Jaramillo-Arango, Jaime (1949). "A critical review of the basic facts in the history of Cinchona". Journal of the Linnean Society of London, Botany. 53 (352): 272–311.
[13] Holmes, Edward Morell (1885). "Remarks on Cinchona ledgeriana as a Species". Journal of the Linnean Society of London, Botany. 21 (136): 374–380.
[14] Russell, Paul F. (1943). "Malaria and its influence on world health". Bulletin of the New York Academy of Medicine. 19 (9): 599–630.
[15] Hesse, Manfred (2002). Alkaloids: Nature's Curse or Blessing?. Wiley-VCH. p. 7.
[16] Van Der Heijden, Robert; Jacobs, Denise I.; Snoeijer, Wim; Hallard, Didier; Verpoorte, Robert (2004). "The Catharanthus alkaloids: Pharmacognosy and biotechnology". Current Medicinal Chemistry. 11 (5): 607–628.
[17] Cooper, Raymond; Deakin, Jeffrey John (2016). "Africa's gift to the world". Botanical Miracles: Chemistry of Plants That Changed the World. CRC Press. pp. 46–51.
[18] Gansäuer, Andreas; Justicia, José; Fan, Chun-An; Worgull, Dennis; Piestert, Frederik (2007). "Reductive C—C bond formation after epoxide opening via electron transfer". In Krische, Michael J. (ed.). Metal Catalyzed Reductive C—C Bond Formation: A Departure from Preformed Organometallic Reagents. Topics in Current Chemistry. 279. Springer Science & Business Media. pp. 25–52.

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