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PLANT USED FOR SKIN CANCER

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ABSTRACT

Plant plays an important role in the treatment of so many disease and now it has shown a tremendous potential in the treatment of cancer. There are various plant part which show greater prospective of treating cancer in the biological system such as whole plant, leaves, bark, roots and fruits yield compound. Plant derived compound have played an important role in the development of several clinically useful anti-cancer agents. These include Turmeric Green Tea, Podophyllum Emodi, Beta Carotene, Paclitaxel, Silybum Marianum. This plant sources are likely to provide effective anticancer agents. This review thus aims at providing an overview of anti-cancer compounds, derived from natural sources. Phytochemicals that are discussed in this review include flavonoids, carotenoids, terpenoids, vitamins, sulforaphane, some polyphenols and crude plant extracts.

KEYWORD: Turmeric, Green Tea, Podophyllum Emodi, Beta Carotene, Paclitaxel, Silybum Marianum.

INTRODUCTON

Plants have been an exemplary source of medicine. Ayurveda and other Indian literature mention the use of plants in treatment of various human ailments. India has about 45,000 plant species and among them, several thousands have been claimed to possess medicinal properties. Traditional system of medicine is found to have utilities as many accounts. Due to population rise adequate supply of drug and high cost of treatment in side effect along with drug resistance has been encountered in synthetic drugs, which has lead to an elevated emphasis for the use of plants to treat human diseases. The affordability of herbals has also drawn the attraction towards their use. India is one of the oldest civilizations which is known

for rich repository of medicinal plants Following plants were investigated for treatment of skin cancer.

1.1Turmeric (Curcuma Longa)

Scientific classification

Kingdom:	Plantae
(unranked):	Angiosperms
(unranked):	Monocots
(unranked):	Commelinids
Order:	Zingiberales
Family:	Zingiberaceae
Genus:	Curcuma
Species:	C. longa

FIGURE : 1 Turmeric

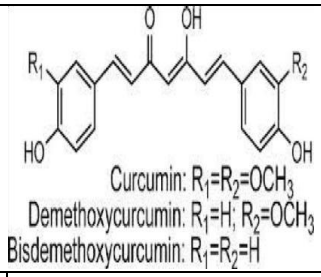

FIGURE : 2 Structure

INTRODUCTION

Turmeric (the common name for curcuma Longa) is an indian spice derived from the rhizomes of the plant and has a long history of use in ayurvedic Medicine as a treatment for inflammatory conditions. C. Longa is a perennial member of the zingiberaceae family And is cultivated in india and other parts of southeast Asia.[17] the primary active constituent of turmeric and The one responsible for its vibrant yellow color is curcumin, First identified in 1910 by lampe and milobedzka.[18] while curcumin has been attributed numerous Pharmacological activities, including antioxidant[19] and Antimicrobial properties,[20] Curcumin's effect on cancer from an anti-inflammatory perspective. on early research conducted with cell cultures and animal models, pilot and clinical trials indicate curcumin may have potential as a therapeutic agent in diseases such as inflammatory bowel disease, pancreatitis, arthritis, and chronic anterior uveitis, as well as certain types of cancer. Turmeric is comprised of a group of three curcuminoids: curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin, as well as volatile oils (tumerone, atlantone, and zingiberone), sugars, proteins, and resins. The curcuminoid complex is also known as Indian saffron.[21] Curcumin is a lipophilic polyphenol that is nearly insoluble in water[22] but is quite stable in the acidic pH of the stomach.[23] A 40 mg/kg intravenous dose of curcumin given to rats resulted in complete plasma clearance at one hour postdose.

Cancer Prevention/Inhibition

Cancer is a hyperproliferative disorder marked by metastasis into the vital organs of the body through invasion and angiogenesis. Curcumin blocks the transformation, proliferation, and

invasion of tumor cells. The biochemical pathways involved in the carcinogenesis process have been investigated extensively over the last four decades. Numerous studies over the last two decades have demonstrated that curcumin targets several steps in these biochemical pathways.

Curcumin suppresses the growth of several tumor cell lines, including drug-resistant lines.[24]

It suppresses the expression of cyclin D1, which is deregulated in a wide variety of tumors. Cyclin D1 is a component subunit of cyclin-dependent kinases (CDK) 4 (Cdk4) and 6 (Cdk6), which are rate limiting in progression of cells through the cell cycle.[25] Curcumin also induces apoptosis in tumor cells by activating caspase-8, which leads to cleavage of Bid, thus resulting in sequential release of mitochondrial cytochrome C and activation of caspase-9 and caspase-3, which leads to activation of poly ADP ribose polymerase (PARP) and apoptosis of tumor cells.

Curcumin also suppresses the activation of several transcription factors that are implicated in carcinogenesis.[26] It suppresses the activation of nuclear factor kappa B (NF-_B), activator protein 1 (AP-1), and at least two of the signal transducer and activator of transcription proteins (STAT3, STAT5), and modulates the expression of early growth response protein 1 (Egr-1), peroxisome proliferatorassociated receptor gamma (PPAR-), _-catenin, and Nrf-2. Curcumin also modulates expression of genes involved in cell proliferation, cell invasion, metastasis, angiogenesis, and resistance to chemotherapy.[27]

Mechanism of Action

Turmeric has been associated with the inhibition of tumor necrosis factor-α, interleukin-8, monocyte inflammatory protein-1, interleukin-1B, and monocyte chemotactic protein-1 25. Turmeric and its constituent curcumin have been found to inhibit lipoxygenase and cyclooxygenase in rat tissues and in vitro.[28,29,30] as well as thromboxane B2 and leukotriene B4 formation[31,32] Based on animal study, oral administration of curcumin may reduce expression of several cytokines, chemokines, and proteinases known to mediate aneurismal degeneration[33] In rat macrophages, curcumin inhibits the incorporation of arachidonic acid into membrane lipids, as well as prostaglandin E2, leukotriene B4, and leukotriene C4, but does not affect the release of arachidonic acid.[34] Curcumin also inhibits the secretion of collagenase, elastase, and hyaluronidase. Inhibition of neutrophil function has been noted[35], and in vitro research demonstrates that curcumin inhibits 5-hydroxy-eicosatetraenoic acid (5-

HETE) in intact human neutrophils. Turmeric has been found to block cytokine-induced transcription of leukocyte adhesion molecules ICAM-1, VCAM-1, and E-selectin[36], and it appears to induce the production of endogenous TGF-B1 in animal wounds.[37] Curcumin down-regulates transcription of genes responsible for the production of chemotactic cytokines in bone marrow stromal cells.[38] Curcumin reduces chemically-induced rat paw edema and liver inflammation demonstrates that curcumin inhibits 5-hydroxy-eicosatetraenoic acid (5-HETE) in intact human neutrophils. Turmeric has been found to block cytokine-induced transcription of leukocyte adhesion molecules ICAM-1, VCAM-1, and E-selectin[36], and it appears to induce the production of endogenous TGF-B1 in animal wounds.[37] Curcumin down-regulates transcription of genes responsible for the production of chemotactic cytokines in bone marrow stromal cells.[38] Curcumin reduces chemically-induced rat paw edema and liver inflammation.

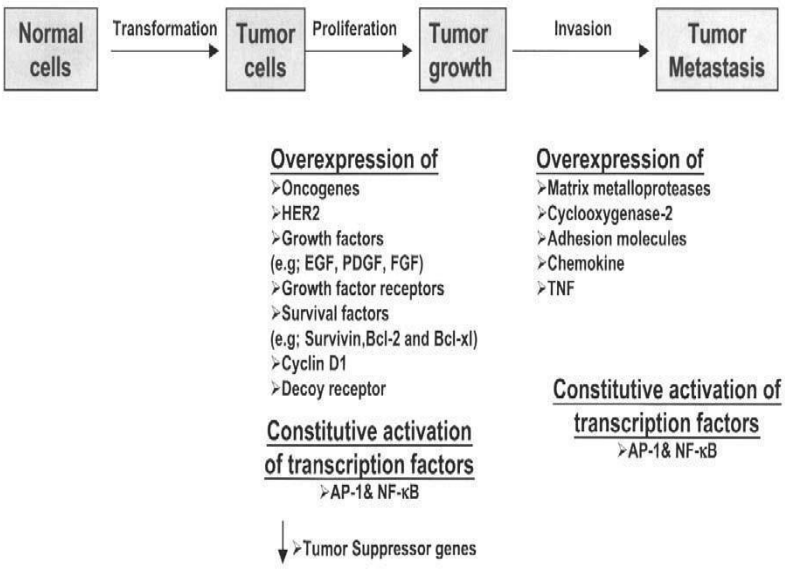

FIGURE: 3 Mechanism of Action

Side Effects and Toxicity

Turmeric usually does not cause significant side effects; however, some people can experience upset, nausea, dizziness, or diarrhea. A person who took very high amounts of turmeric, over 1500 mg twice daily, experienced a dangerous abnormal heart rhythm. However, it is unclear if turmeric was the actual cause of this side effect. Pregnancy and breast-feeding: Taking turmeric by mouth in medicinal amounts is likely unsafe in pregnancy. It might promote a menstrual period or stimulate the uterus, putting the pregnancy at risk. Don't take turmeric if you are pregnant.

Dosage

By mouth: For upset stomach (dyspepsia): 500 mg of turmeric four times daily. For osteoarthritis: 500 mg twice daily of a specific turmeric extract (Meriva, Indena); 500 mg four times daily of a non-commercial product has also been used.

For rheumatoid arthritis (RA): 500mg twice daily of a specific formulation of the turmeric constituent, curcumin (BCM-95®, Arjuna Natural Extracts, India), has been used.

In some instances, turmeric extract is applied directly over the skin. This can result in allergic reactions of the skin, which generally are minor and go away quickly. People might notice rashes, irritation and swelling of the skin where the turmeric was applied.

1.2 Green Tea (Camellia sinensis)

Scientific classification

Kingdom: Plantae	
(unranked): Angiosperms	
(unranked): Eudicots	
(unranked): Asterids	
Order: Ericales	
Family: Theaceae	
Genus: Camellia	
Species: C. sinensis	**FIGURE : 4 Green Tea (Camellia sinensis)**

Introduction

Tea is one of the most widely consumed beverages in the world, second only to water, and its medicinal properties have been widely explored. The tea plant, Camellia sinensis, is a member of the Theaceae family, and black, oolong, and green tea are produced from its leaves. It is an evergreen shrub or tree and can grow to heights of 30 feet, but is usually pruned to 2-5 feet for cultivation. The leaves are dark green, alternate and oval, with serrated edges, and the blossoms are white, fragrant, and appear in clusters or singly. It is prepared from unfermented leaves compared to the leaves of oolong tea which are partially fermented and black tea which are fully fermented. Green tea is rich in varieties of beneficial chemicals with maximum positive effects on human beings.

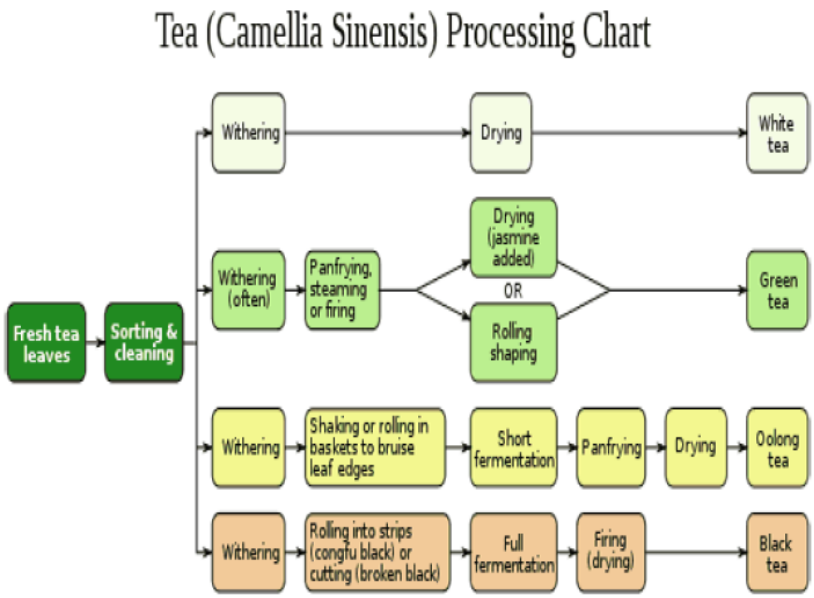

FIGURE: 5 Processing Chart

Active Constituents

Green tea is produced from steaming fresh leaves at high temperatures, thereby inactivating the oxidizing enzymes and leaving the polyphenol content intact. The polyphenols found in tea are more commonly known as flavanols or catechins, and comprise 30-40 percent of the extractable solids of dried green tea leaves. The main catechins in green tea are epicatechin, epicatechin-3gallate, epigallocatechin, and epigallocatechin-3-gallate (EGCG), with the latter being the highest in concentration. Green tea polyphenols have demonstrated significant antioxidant, anticarcinogenic, anti-inflammatory, thermogenic, probiotic, and antimicrobial properties in numerous human, animal. Other compounds are alkaloids (caffeine, theophylline and theobromine), amino acids, carbohydrates, proteins, chlorophyll, volatile organic compounds (chemicals that readily produce vapors and contribute to the odor of tea), fluoride, plant aluminum, minerals and trace elements.[40] There are active hydroxyl hydrogens in the molecular structure of green tea polyphenols that can end the chain reaction of excessive free radicals that (otherwise) result in pathological changes in the human body.

Mechanisms of Action

The anticarcinogenic properties of green tea polyphenols, mainly EGCG, are likely a result of inhibition of tumor initiation and promotion, induction of apoptosis, and inhibition of cell replication rates, thus retarding the growth and development of neoplasms.[41,42] Green tea polyphenols' antioxidant potential is directly related to the combination of aromatic rings

and hydroxyl groups that make up their structure, and is a result of binding and neutralization of free radicals by the hydroxyl groups. In addition, green tea polyphenols stimulate the activity of hepatic detoxification enzymes, thereby promoting detoxification of xenobiotic compounds, and are also capable of chelating metal ions, such as iron, that can generate radical oxygen species.[43,44] Green tea polyphenols inhibit the production of arachidonic acid metabolitessuch as pro-inflammatory prostaglandins and leukotrienes, resulting in a decreased inflammatory response. Human and animal studies have demonstrated EGCG's ability to block inflammatory responses to ultraviolet A and B radiation, as well as significantly inhibiting neutrophil migration that occurs during the inflammatory process.[45,46,47] On green tea's thermogenic properties indicates a synergistic interaction between its caffeine content and catechin polyphenols that can result in prolonged stimulation of thermogenesis. Green tea extracts are capable of reducing fat digestion by inhibiting the activity of certain digestive enzymes.[48,49] Green tea catechins have been shown to significantly raise levels of Lactobacilli and Bifidobacteria while decreasing levels of numerous potential pathogens.[50]

Cancer Prevention/Inhibition

Green tea polyphenols' preventative and inhibitory effects against tumor formation and growth. green tea polyphenols, particularly EGCG, may be effective in preventing cancer of the prostate, breast, esophagus, stomach, pancreas, and colon.[51] There is also some evidence that green tea polyphenols may be chemopreventive or inhibitory toward lung, skin, and liver cancer.[52,53,54] bladder and ovarian tumors,[55,56] leukemia,[57] and oral leukoplakia.[58]

Side Effects and Toxicity

Green tea is generally considered a safe, non-toxic beverage and consumption is usually without side effects. The average cup of green tea contains from 10-50 mg of caffeine, and overconsumption may cause irritability, insomnia, nervousness, and tachycardia. its possible teratogenic effect are inconclusive, caffeine consumption is contraindicated during pregnancy.

Lactating women should also limit caffeine intake to avoid sleep disorders in infants.[59]

Dosage

The dosage for green tea beverage varies, depending on the clinical situation and desired therapeutic effect. The phenolic content of green tea infusion is between 50-100 mg polyphenols per cup, depending on species, harvesting variables, and brewing methods,[60] with typical dosages range from 3 to 10 cups per day. Cancer preventative effects are usually associated with dosages in the higher end of the range.[61] Green tea extracts standardized to 80-percent total polyphenols are dosed at 500-1,500 mg per day.

1.3 Podophyllum Emodi

Scientific classification

Kingdom: Plantae	
Division: Magnoliophyta	
Class: Magnoliopsida	
Order: Ranunculales	
Family: Berberidaceae	
Genus: Podophyllum	
Species: P. hexandrum	

FIGURE: 6 Podophyllum emodi

Introduction

The perennial herb Podophyllum hexandrum (syn. P. emodi), bearing the common names Himalayan mayapple or Indian may apple, is native to the lower elevations in and surrounding the Himalaya. It is low to the ground with glossy green, drooping, lobed leaves on its few stiff branches, and it bears a pale pink flower and bright red-orange bulbous fruit. The ornamental appearance of the plant make it a desirable addition to woodland-type gardens. It can be propagated by seed or by dividing the rhizome. It is very tolerant of cold temperatures, as would be expected of a Himalayan plant, but it is not tolerant of dry conditions. Its name in Hindi and Ayurveda is bantrapushi or Giriparpat.[62] Podophyllotoxin is the starting material for the semisynthesis of the anti-cancer drugs etoposide, teniposide and etopophos. These compounds have been used for the treatment of lung and testicular cancers as well as certain leukemias. It is also the precursor to a new derivative CPH 82 that is being tested for rheumatoid arthritis in Europe, and it is the precursor to other derivatives used for the treatment of psoriasis and malaria. Several podophyllotoxin preparations are on the market for dermatological use to treat genital warts. Since the total synthesis of podophyllotoxin is an expensive process, availability of the compound from natural renewable resources is an important issue for pharmaceutical companies that manufacture these drugs.The commercial

source of podophyllotoxin is the rhizomes and roots of Podophyllum emodi Wall. (syn. P. hexandrum Royle), Berberidaceae, an endangered species from the Himalayas. The leaf blades of the North American mayapple (P. peltatum L.) may serve as an alternative source of podophyllotoxin production. leaves are renewable organs that store lignans as glucopyranosides, podophyllotoxin can be obtained by conversion of podophyllotoxin 4-O- -D- glucopyranoside into the aglycone using our buffer extraction procedure. This extraction procedure of P. peltatum leaves yields podophyllotoxin in amounts similar to the ethanol extraction of P. emodi rhizomes and roots.

Active Constituents

It is derived from the phenylpropanoid pathway, which are ubiquitously distributed among plant species and play important roles in plant defense. The aryltetralin lignans are found in high amounts in plants of the genus Podophyllum. podophyllotoxin is the most important due its biological activity blocking mitosis and its use as the starting compound of the semi-synthetic chemotherapeutic drugs etoposide, teniposide, and etopophos. These antineoplastic pharmaceuticals block DNA toposisomerase II Minocha and Long 1984) and have been used for the treatment of small and large cell lung, refractory testicular, stomach, pancreatic cancers, and myeloid leukemias.

Mechanism of Action

The applicable parts of podophyllum are the root, rhizome, and resin. Podophyllin resin is obtained from the rhizome. The major active constituents in podophyllum resin are podophyllotoxin, quercetin and kampherol. Podophyllum seems to be cytotoxic by interrupting cellular mitosis at metaphase. Podophyllum seems to increase the incorporation of amino acids into proteins, and inhibit purine synthesis and incorporation of purines into RNA. It also seems to inhibit mitochondrial function. The oncologic drugs etoposide (Etophophos) and teniposide (Vumon) are a semisynthetic derivative of podophyllotoxin. The flavonoids quercetin and mutagenic. Preliminary research suggests that an aqueous extract of podophyllum, quercetin, and podophyllotoxin might have antioxidant effects and protect against radiation damage. These podophyllum constituents also seem to increase apoptosis (cell death) and phagocytosis of cells damaged by radiation, making way for new cells.

Side Effects and Toxicity

In toxic doses, podophyllin causes intense enteritis, with all its characteristic symptoms, and severe depression, which may end in death. The treatment is symptomatic, there being no specific antidote. Even when podophyllin resin is used topically, it can be systemically absorbed into the body, and fatal and near-fatal reactions have been reported, particularly when it is used extensively or on mucous membranes. Neither podophyllin resin nor podofilox lotion or gel is used during pregnancy because these medications can be harmful to the fetus. The most common side effects near the application site are skin reactions, including burning, redness, pain, itching, swelling. There is some concern about the mutagenicity of some of the flavonoids in podophyllin.

Dosage

Podophyllum resin, as a 10% to 25% suspension in tincture of benzoin, is applied to an area no more than 10 square cm, with protection of surrounding skin to minimize toxicity. It should be washed off four to six hours after application . Podophyllum should not be used for selftreatment. Podophyllotoxin 0.5% gel is applied twice daily for three consecutive days and repeated for two to four cycles. It is considered safe for patient application.

1.4 β-carotene (beta-carotine)

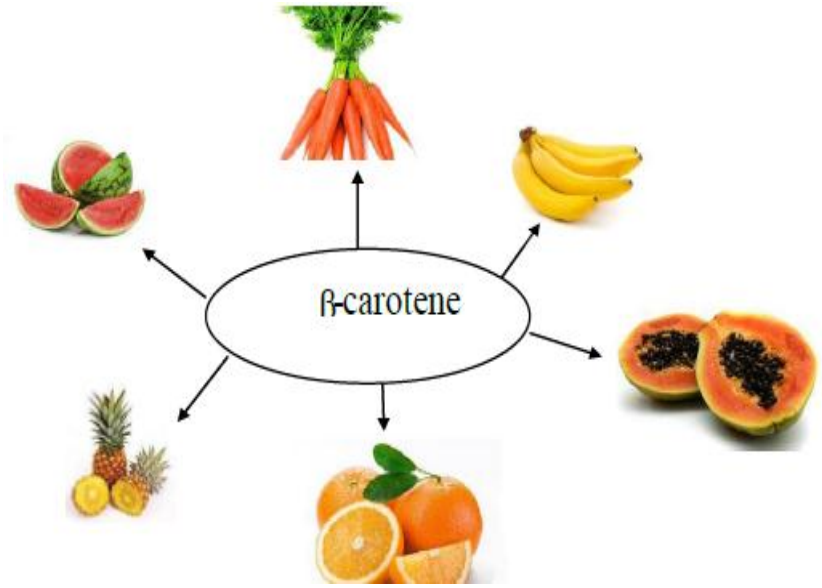

FIGURE: 7 β-carotene

Introduction

β-carotene (beta-carotine) is a strongly colored red-orange pigment abundant in plants and fruits. It is an organic compound and chemically is classified as a hydrocarbon and

specifically as a terpenoid (isoprenoid), reflecting its derivation from isoprene units. β-Carotene is biosynthesized from geranylgeranyl pyrophosphate.[63] It is a member of the carotenes, which are tetraterpenes, synthesized biochemically from eight isoprene units and thus having 40 carbons. Among this general class of carotenes, β-carotene is distinguished by having beta-rings at both ends of the molecule. Absorption of β-carotene is enhanced if eaten with fats, as carotenes are fat soluble.

Carotene is the substance in carrots, pumpkins and sweet potatoes that colors them orange and is the most common form of carotene in plants. When used as a food coloring, it has the E number E160a.[64] In nature, β-carotene is a precursor (inactive form) to vitamin A via the action of beta- carotene-monooxygenase.[65] Isolation of β-carotene from fruits abundant in carotenoids is commonly done using column chromatography. The separation of β-carotene from the mixture of other carotenoids is based on the polarity of a compound. β-Carotene is a non-polar compound, so it is separated with a nonpolar solvent such as hexane.[66] Being highly conjugated, it is deeply colored, and as a hydrocarbon lacking functional groups, it is very lipophilic.

The name "carotene" was first coined in the early 19th Century by the scientist Wachenroder after he crystallized this compound from carrot roots. Beta-carotene is a member of the carotenoids, which are highly pigmented (red, orange, yellow), fat-soluble compounds naturally present in many fruits, grains, oils, and vegetables (green plants, carrots, sweet potatoes, squash, spinach, apricots, and green peppers). Alpha, beta, and gamma carotene are considered provitamins because they can be converted to active vitamin A.

Active Constituents

The name "carotene" was first coined in the early 19th Century by the scientist Wachenroder after he crystallized this compound from carrot roots. Beta-carotene is a member of the carotenoids, which are highly pigmented (red, orange, yellow), fat-soluble compounds naturally present in many fruits, grains, oils, and vegetables (green plants, carrots, sweet potatoes, squash, spinach, apricots, and green peppers). Alpha, beta, and gamma carotene are considered provitamins because they can be converted to active vitamin A.

Mechanism of Action

Lycopene has the capacity to prevent free radical damage to cells caused by reactive oxygen species.[67] It is a potent antioxidant in vitro and in human studies, reducing the susceptibility

of lymphocyte DNA to oxidative damage,[68] inactivating hydrogen peroxide and nitrogen dioxide,14 and protecting lymphocytes from nitrogen oxideinduced membrane damage and cell death twice as efficiently as beta-carotene.[69] mechanisms of action for lycopene, including modulation of intercellular gap junction communication, an anticancer mechanism.[68,69] In addition, lycopene at physiological concentrations has been shown to inhibit human cancer cell growth by interfering with growth factor receptor signaling and cell cycle progression, specifically in prostate cancer Cells.[70]

Clinical Indications

Oxidative stress is recognized as one of the major contributors to increased risk of cancer, and in chemical assays lycopene is the most potent antioxidant among various common carotenoids.[71] Lycopene has been found to inhibit proliferation of several types of human cancer cells, including endometrial, breast, and lung.[72,73,74] It is debated whether β-carotene is effective in treating different forms of cancer and it has not currently been proven to prevent cancer in humans.[75] Studies have shown that patients with cervical intraepithelial neoplasia (CIN) respond favorably to β-carotene supplementation[76] however, high levels of β-carotene have also been found to increase the risk of lung cancer in current and former smokers.[77] β-Carotene is used to help prevent breast cancer although there are currently no findings to support that diets high in β- carotene are associated with lower breast cancer risk.

Side Effects and Toxicity

Lycopene is generally considered safe, non-toxic, and consumption is usually without side effects. Scientific evidence for lycopene use in pregnancy is not available; however, no adverse events have been reported in association with the consumption of lycopene-containing foods during pregnancy. Obtaining lycopene from food sources, rather than supplements, during pregnancy and while nursing has been suggested.[80]

Dosage

Therapeutic dosages of lycopene range from 6-60 mg daily. Dosages cited in the literature include 6 mg for reducing the risk of prostate cancer[81] 6.5 mg for reducing the risk of lung cancer in non-smoking women[82] 12 mg for reducing the risk of lung cancer in non-smoking men[82] 30 mg for decreasing the growth of prostate cancer[83] and preventing exercise-induced asthma[84] and 60 mg for reducing LDL cholesterol.[85]

1.5 Paclitaxel

Scientific classification

Kingdom:	Plantae
Division:	Pinophyta
Class:	Pinopsida
Order:	Pinales
Family:	Taxaceae
Genus :	Taxus
Species:	T. baccata
Binomial:	Taxus baccata

FIGURE: 8 Taxus baccata

Introduction

Paclitaxel is a mitotic inhibitor used in cancer chemotherapy. It was discovered in a US National Cancer Institute program at the Research Triangle Institute in 1967 when Monroe E. Wall and Mansukh C. Wani isolated it from the bark of the Pacific yew tree, Taxus brevifolia and named it taxol. Later it was discovered that endophytic fungi in the bark synthesize paclitaxel. When it was developed commercially by Bristol-Myers Squibb (BMS), the generic name was changed to paclitaxel and the BMS compound is sold under the trademark Taxol. In this formulation, paclitaxel is dissolved in Kolliphor EL and ethanol, as a delivery agent. A newer formulation, in which paclitaxel is bound to albumin, is sold under the trademark Abraxane.

Paclitaxel is a natural product with antitumor activity. TAXOL (paclitaxel) is obtained via a semi- synthetic process from Taxus baccata. The chemical name for paclitaxel is 5β,20-Epoxyl,2α,4,7β,10β,13α-hexahydroxytax-l l-en-9-one 4,10-diacetate 2-benzoate 13-ester with (2R,3S)N-benzoyl-3-phenylisoserine. Paclitaxel is a white to off-white crystalline powder with the empirical formula $C_{47}H_{51}NO_{14}$ and a molecular weight of 853.9. It is highly lipophilic, insoluble in water, and melts at around 216-217° C. Paclitaxel is used to treat patients with lung, ovarian, breast, head and neck cancer, and advanced forms of Kaposi's sarcoma. Paclitaxel is also used for the prevention of restenosis. Paclitaxel stabilizes microtubules and, as a result, interferes with the normal breakdown of microtubules during cell division. Together with docetaxel.

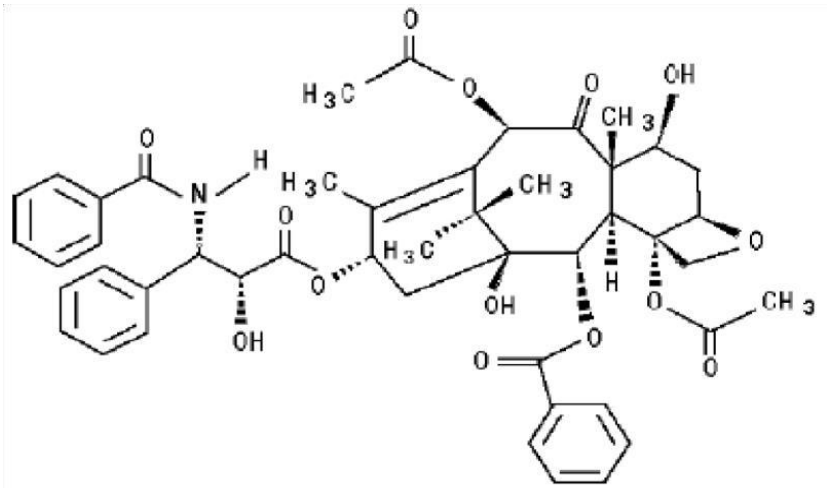

FIGURE: 9 Structure (Paclitaxel)

Active Constitutent

Paclitaxel produced was derived from bark from the Pacific yew, the harvesting of which kills the tree in the process. The processes used were descendants of the original isolation method. It had been clear for many years that an alternative, sustainable source of supply would be needed. Initial attempts used needles from the tree, or material from other related Taxus species, including cultivated ones, but these attempts were bedevilled by the relatively low and often highly variable yields obtained. It was not until the early 1990s, at a time of increased sensitivity to the ecology of the forests of the Pacific Northwest, that taxol was successfully extracted on a clinically useful scale from these sources.[86]

Mechanism of action

Paclitaxel is one of several cytoskeletal drugs that target tubulin. Paclitaxel-treated cells have defects in mitotic spindle assembly, chromosome segregation, and cell division. Unlike other tubulin-targeting drugs such as colchicine that inhibit microtubule assembly, paclitaxel stabilizes the microtubule polymer and protects it from disassembly. Chromosomes are thus unable to achieve a metaphase spindle configuration. This blocks progression of mitosis, and prolonged activation of the mitotic checkpoint triggers apoptosis or reversion to the G-phase of the cell cycle without cell division.[87][88] The ability of paclitaxel to inhibit spindle function is generally attributed to its suppression of microtubule dynamics,[89] but recent studies have demonstrated that suppression of dynamics occurs at concentrations lower than those needed to block mitosis. At the higher therapeutic concentrations, paclitaxel appears to suppress microtubule detachment from centrosomes, a process normally activated during mitosis.[90] The binding site for paclitaxel has been identified on the beta-tubulin subunit.[91]

Side Effect

Common side effects include nausea and vomiting, loss of appetite, change in taste, thinned or brittle hair, pain in the joints of the arms or legs lasting two to three days, changes in the color of the nails, and tingling in the hands or toes. More serious side effects such as unusual bruising or bleeding, pain/redness/swelling at the injection site, change in normal bowel habits for more than two days, fever, chills, cough, sore throat, difficulty swallowing, dizziness, shortness of breath, severe exhaustion, skin rash, facial flushing,female infertility by ovarian damage[92] and chest pain can also occur. A number of these side effects are associated with the excipient used, Cremophor EL, a polyoxyethylatedcastor oil. Allergies to drugs such as cyclosporine, teniposide and drugs containing polyoxyethylated castor oil may indicate increased risk of adverse reactions to paclitaxel.[93] Dexamethasone is given prior to beginning paclitaxel treatment to mitigate some of the side effects Leuprolide, a GnRH analog may prevent ovarian damage.

1.6 Silybum Marianum

Scientific classification

Kingdom:	Plantae
(unranked):	Angiosperms
(unranked):	Eudicots
(unranked):	Asterids
Order:	Asterales
Family:	Asteraceae
Tribe:	Cynareae
Genus:	Silybum
Species:	S. marianum
Binomial name: Silybum marianum	
Synonyms :	Carduus marianus L.

FIGURE : 10 Silybum Marianum

Introduction

Silybum marianum (milk thistle) has been used for centuries as an herbal medicine for the treatment of liver disease. Its use for liver disorders dates back to Pliny the Elder, a Roman naturalist, who described milk thistle as being “excellent for carrying off bile.” Milk thistle is an annual or biennial plant indigenous to Europe and is also found in some parts of the United States. It grows in rocky soils to a height of three to ten feet with an erect stem that bears large, alternating, prickly-edged leaves. The common name, milk thistle, is derived from the “milky white” veins on the leaves, which, when broken open, yield a milky sap. Flowering season is from June to August, and each stem bears a single, large, purple flower ending in sharp

spines. The fruit portion of the plant is glossy brown or gray with spots[94] Modern extracts of the plant are produced from the small hard fruits that have the feathery tuft (known as the pappus) removed.

Active Constituents

A flavonolignan complex in milk thistle fruit was identified and isolated. Named silymarin, this complex was found to be responsible for the medicinal benefits of the plant.[95] The silymarin complex is made up of three parts: silibinin (also called silybin), silydianin, and silychristin. Silibinin is the most active of the three, and is largely responsible for the hepatoprotective benefits attributed to silymarin.[96][97] Milk thistle fruit contains 1.5-3.0 percent flavonolignans.

Mechanisms of Action

Silymarin, and more specifically silibinin, directly aids hepatocytes by binding to the outside of the cells and blocking the binding of potential hepatocellular toxins. This was first noted in experimental studies investigating toxins from Amanita phalloides (death cap mushroom).[98][99] Ingesting this mushroom causes swift and severe damage to hepatocytes. Silymarin blocks the receptor sites by which the mushroom toxins enter the cells. In addition, toxins that have already penetrated hepatocytes are neutralized by silibinin. In animal studies, silymarin given within 10 minutes after Amanita toxin ingestion completely counteracted the toxic effects, and if given within 24 hours of toxin ingestion silymarin prevented death and greatly reduced liver damage.[100] Similar hepatoprotective effects have been shown in in vitro and animal studies against ethanol and acetaminophen.[101][102]

Side Effects and Toxicity

Milk thistle extract is virtually devoid of any side effects and may be used by a wide range of people, including pregnant and lactating women. Since silymarin does have some choleretic activity, it may have a mild, transient laxative effect in some individuals. This will usually cease within two or three days.

Dosage

The standard dosage of milk thistle extract, standardized to 70-80 percent silymarin, is 140 milligrams of silymarin three times daily. In persons with liver disease, it is recommended that this dose be used until clinical improvement is verified by laboratory tests. According to research and clinical experience, improvement should be noted in about eight weeks.

However, in persons with chronic liver disease due to hepatitis or cirrhosis, ongoing use of silymarin may be necessary.

CONCLUSION

Plants have played a remarkable role in health care since the ancient times. Traditional plant based medicines still exert a great deal of importance to people living in developing countries and also lead to discovery of new drug candidates. There are lots of medicinal plants available in nature which has the anticancerous properties and majority of them are still to be explored for its anti cancer property. Use of natural compounds in cancer treatment is relatively cheap due to the availability of plants and the simple methods used in product preparation.

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