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Pharmacognosy of Clove & Digitallis

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Introduction

Digitalis is a substance derived from the dried leaves of the common foxglove plant, Digitalis purpurea, that is used to treat certain heart conditions. History Digitalis has been used in clinical medicine for over two centuries. It was first included in the Edinburgh Pharmacopoeia in 1744, and in the Paris Pharmacopoeia in 1748.Digitalis increases the amount of calcium in the heart's cells, slows the signals that start in the sinoatrial (SA) node, and binds to sodium and potassium receptors in the heart muscle. Digitalis is used to treat congestive heart failure, atrial fibrillation, and other heart conditions. Side effects Digitalis can cause side effects such as irregular heartbeat, palpitations, shortness of breath, sweating, fainting, skin rash or hives, and headache.

Symptoms of toxicity include nausea, vomiting, visual changes, arrhythmia, headache, malaise.

Digitalis is used to treat congestive heart failure (CHF) and heart rhythm problems (atrial arrhythmias). Digitalis can increase blood flow throughout your body and reduce swelling in your hands and ankles.

Digitalis Purpurea

The colours of the petals of the *Digitalis purpurea* are known to be determined by at least three genes that interact with each other. The M gene determines the production of a purple pigment, a type of anthocyanin. The m gene does not produce this pigment. The D gene is an enhancer of the M gene, and leads it to produce a large amount of the pigment. The d gene does not enhance the M gene, and only a small amount of pigment is produced. Lastly, the W gene causes the pigment be deposited only in some spots, while the w gene allows the pigment to be spread all over the flower.

Extracted from the leaves, this same cardiac glycoside digitoxin is used as a medication for heart failure. Its clinical use was pioneered by William Withering, who recognized it "reduced dropsy", increased urine flow, and had a powerful effect on the heart. During World War II, County Herb Committees were established to collect medicinal herbs when German blockades created shortages; this included *Digitalis purpurea* which

was used to regulateheartbeat.

SCIENTIFIC CLASSIFICATION

The *Flora Europaea* originally recognised a number of species now seen as synonyms of *Digitalis purpurea*, or others:

- Digitalis atlantica
- Digitalis canariensis L.
- Digitalis cariensis
- Digitalis cedretorum
- Digitalis chalcantha
- Digitalis ciliata Trautv.
- Digitalis davisiana
- Digitalis ferruginea L.
- Digitalis fuscescens
- Digitalis grandiflora Mill.
- Digitalis ikarica
- Digitalis isabelliana
- Digitalis laevigata
- Digitalis lamarckii Ivanina
- Digitalis lanata
- Digitalis lutea L.
- Digitalis mariana
- Digitalis minor L.
- Digitalis nervosa
- Digitalis obscura L.
- Digitalis parviflora Jacq.
- Digitalis purpurea L.
- Digitalis sceptrum L.f.
- Digitalis subalpina

- Digitalis thapsi L.
- Digitalis transiens
- Digitalis viridiflora

SYNONYMS

- Digitalis lutea.
- Digitalis purpurea.
- common foxglove.
- fairy bell.
- finger-flower.
- finger-root.
- fingerflower.
- fingerroot

DESCRIPTION

A popular ornamental plant with bell-shaped flowers that can be purple, yellow, white. The flowers grow in a cluster on one side of the stem, and the plant can grow to be 18–60 in tall. Most species are biennials, meaning they flower in their second year and then die after seeding**.** A cardiac glycoside derived from the dried leaves of the foxglove plant. It's used to make drugs that treat heart conditions like congestive heart failure and atrial arrhythmias. Digitalis works by increasing the amount of calcium in the heart's cells, slowingsignals in the heart, and binding to receptors in the heart muscle.

Digitalis can cause side effects like irregular heartbeat, palpitations, shortness of breath, sweating, fainting, skin rash, and headache. Toxicity can occur if too much of the drug is taken at once, or if levels build up for other reasons. Digoxin is the most common prescription form of digitalis. Treatment for digitalis toxicity usually involves administering digoxin-specific Fab.

Foxglove is a pinkish purple flower which can grow up to 2m tall. Foxgloves are an important source of pollen for bees. Its leaves are oval-shaped and hairy with a toothed margin. These flowers grow in gardens, woodland edges, heathland and roadside verges.

ECOLOGY

Habitat: Foxgloves grow in a variety of habitats, including open woods, woodland

clearings, moorland, sea-cliffs, and rocky mountain slopes. They prefer acidic soils that are humus-rich, but can grow in any soil that isn't too wet or too dry. They are often found in areas where the ground has been disturbed, such as recently cleared woodlandor construction sites.

Reproduction: Foxgloves reproduce sexually through pollination by insects like bees and hummingbirds. The shape of the flower's tube makes it attractive to long-tongued bees, which are likely to drop pollen from other foxgloves when landing on the flower.

Ornamental value: The flowers of the foxglove are eaten by the larvae of the foxglove pug moth, while the leaves are eaten by other species of Lepidoptera. Foxgloves are cultivated for their ornamental value and to attract bumblebees to gardens.

Figure2: Digoxin Tablets, USP

CULTIVATION

Digitalis, also known as foxglove, can be cultivated in a number of ways, including:

- **Soil**: Digitalis grows best in well-drained, slightly acidic, sandy soil that's rich in organic matter. It can also grow in limestone soil.
- **Climate**: Digitalis prefers a cool, mild climate with temperatures between 20–30°C. It can grow at elevations above 1250 meters.
- **Sunlight**: Digitalis can grow in partial sunlight to deep shade.
- **Propagation**: Digitalis can be propagated by seed. Seeds can be sown directly in the field or raised in a nursery and then transplanted.
- **Planting**: The optimal seed rate for direct sowing is 8 kg/ha, and 2 kg/ha for transplanting. Seeds should be planted at a spacing of 45 x 30 cm.
- **Fertilizing**: To get a good yield, provide balanced nutrients. This can include farmyard

manure or compost, nitrogen, phosphorous, and potash.

- **Weeding**: Weed the plant 1–2 times in the initial stages.
- **Harvesting**: Leaves can be harvested between July and August from the first-yearcrop. The second harvest can be taken one and a half months later. Leaves should be collected when 2/3rd of the flowers are fully developed.
- **Drying**: Leaves can be dried by passing hot air at 60°C.

EXTRACTION

Soxhlet Apparatus

D. purpurea L. leaves in the third year were collected in the medicinal botanical garden (Kanazawa, Japan) of this University. The leaves were quickly washed with water and dried under reduced pressure at room temperature for 2 weeks. The dried leaves were pulverized and then sifted through a sieve of mesh width 500 pm. Approximately 50 mg of leaf powder were accurately weighed and extracted with 120 ml of ethanol-chloroform (2:1) containing an internal standard (0.09149 mg) in a Soxhlet apparatus for 4 h. The extract obtained was evaporated to dryness using a rotary evaporator and partitioned between chloroform (35 ml) and water (20 ml) saturated with sodium chloride in a separatory funnel. The chloroform fraction was concentrated in vacua and successively partitioned between cyclohexane (40 ml) and methanol-water (4: l) (45 ml). The methanol of the aqueous layer was removed and further re-extracted with chloroform (35 ml). After evaporation of the solvent, the residue was submitted to preparative TLC on

silica gel using cyclohexane-chloroform-methanol (3:3:1) as developing solvent. The adsorbent corresponding to RF 0.15-0.4 was eluted with ethylacetate and the eluate was then evaporated in vacua. The material was redissolved in the mobilephase (0.1 ml) and 0.3 ~1 of the solution was injected into the liquid chromatography.

PHYTOCHEMICAL TEST

Digitalis contains a variety of phytochemicals, including:

- **Cardiac glycosides**: These are the most important phytochemicals in Digitalis and are responsible for its cardiovascular effects. Some examples of cardiac glycosides include digitoxin, digoxin, ouabain, oleandrin, and proscillaridin.
- **Flavonoids**: These can be detected by a yellow colour that turns colourless when hydrochloric acid is added.
- **Saponins**: These can be detected by a foam test.
- **Anthraquinones**: These can be detected by a red colour when the Borntrager test is performed.
- **Carbohydrates**: These can be detected by a purple ring when Molisch's reagent is added.
- **Steroids**: These can be detected by the Salkowski test.

ADVERSE EFFECT

Symptoms may be mild and include nausea, vomiting, and anorexia. Visual side effects might include color changes, also known as xanthopsia. However, yellow or green-tinted vision is usually associated with digoxin toxicity. Patients may also highlight blurry vision or photopsia. At toxic levels, digoxin is proarrhythmic. An impaired ventricle is more prone to ventricular tachyarrhythmias and ectopy. Abnormally high digoxin levels stimulate atrial activation; thus, atrial tachycardias in a patient on digoxin is highly suggestive of toxicity. These atrial tachycardias are persistent and resolve with a decrease in serum digoxin levels.

Digoxin toxicity is clinically relevant as it can lead to fatal cardiac arrhythmias. The estimated frequency is about 0.8 to 4% of patients on steady digoxin therapy. The rate of toxicity increasesas serum digoxin concentration reaches over 2.0 ng/mL. However, toxicity can also occur at lower levels, especially in the setting of other risk factors such as low body weight, advanced age, decreased renal function, and hypokalemia

Other common side effects include:

- Rash
- Headache

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- Gynecomastia
- Weakness

HEALTH BENEFITS OF DIGITALIS

Foxglove (Digitalis purpurea, Digitalis lanata) is a plant. It is the source of the modern drug, digoxin. All parts of the plant are poisonous. The chemicals in foxglove can increase the strength of heart muscle contractions, change heart rate, and increase heart blood output.

MECHANISM OF ACTION

Digoxin's primary mechanism of action is to inhibit the sodium-potassium adenosine triphosphatase (ATPase) pump in the heart, which increases intracellular calcium levels:

- **Increased intracellular calcium**

  Inhibition of the sodium-potassium ATPase pump causes a build-up of intracellular sodium, which is then exchanged for calcium ions. This increase in calcium helps the heart contract more forcefully.

- **Decreased heart rate:**

  Digoxin also has a parasympathetic effect on the heart, which slows the electrical conduction in the atrioventricular (AV) node and decreases the heart rate.

- **Neurohormonal effects:**

  Digoxin can improve baroreceptor sensitivity, decrease norepinephrine concentration, and decrease activation of the renin-angiotensin system.

SIDE EFFECTS

Digoxin can cause a variety of side effects, including:

- Cardiac arrhythmias, such as atrial fibrillation, ventricular fibrillation, and premature ventricular contractions
- Gastrointestinal upset
- Visual disturbances, such as a yellow-green discoloration
- Dizziness or fainting

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CONTRAINDICATIONS

Digoxin is contraindicated in the following conditions:

- Acute myocardial infarction.
- Hypersensitivity to the drug.
- Ventricular fibrillation.
- Myocarditis.
- Hypomagnesemia.
- Hypokalaemia.
- Wolf-Parkinson-White syndrome

Clove

Introduction

Spices as clove, oregano, mint, thyme and cinnamon, have been employed for centuries as food preservatives and as medicinal plants mainly due to its antioxidant and antimicrobial activities. Nowadays, many reports confirm the antibacterial, antifungal, antiviral and anticarcinogenic properties of spice plants. Clove in particular has attracted the attention due to the potent antioxidant and antimicrobial activities standing out among the other spices. Syzygium aromaticum (S. aromaticum) (synonym: Eugenia Cariophylata) commonly known as clove, is a median size tree (8-12 m) from the Vitaceae family native from the Maluku islands in east Indonesia. For centuries the trade of clove and the search of this valuable spice stimulated the economic development of this Asiatic region. The clove tree is frequently cultivated in coastal areas at maximum altitudes of 200 m above the sea level. The production of flower buds, which is the commercialized part of this tree, starts after 4 years of plantation. Flower buds are collected in the maturation phase before flowering. The collection could be done manually or chemically-mediated.

Clove Plant

Nowadays, the larger producer countries of clove are Indonesia, India, Malaysia, Sri Lanka, Madagascar and Tanzania specially the Zanzibar Island. In Brazil, clovis cultured in the northeast region, in the state of Bahia in the regions of Valença, Ituberá, Taperoá, Cadmium and Nalo Peçanha, where approximately 8 000 hectares are cultivated, producing near 2 500 tons peryear.

SCIENTIFIC CLASSIFICATION

Name: Syzygium aromaticum

Kingdom: Plantae **Class:** Angiosperms **Request:** Myrtales **Family:** Myrtaceous **Class:** Syzygium **Species:** S. aromaticum

SYNONYMS

- Caryophyllus aromatics
- Eugenia aromatic
- Eugeniac caryophyllata

DESCRIPTION

Cloves are a spice that comes from the dried flower buds of the Syzygium aromaticum

tree andare described as:

- **Appearance**: Small, round-headed nails that are blackish brown in colour and about 10–17.5 mm long
- **Taste**: Hot and pungent with a strong aroma
- **Uses**: A key ingredient in many Asian foods, including curries, seasoned meats, Worcestershire sauce, baked goods, chai, and Chinese five-spice blends
- **Health benefits**: Rich in antioxidants, may protect against cancer cell growth, kill harmful bacteria, regulate blood sugar levels, improve bone health, reduce stomach ulcers, cure oral problems, and improve liver health

Cloves are native to Indonesia, but are now also found in Sri Lanka and the Moluccas. They canbe used whole or ground. The clove tree is an evergreen that grows to about 8 to 12 metres (25 to 40 feet) in height. Its gland-dotted leaves are small, simple, and opposite. The trees are usually propagated from seeds that are planted in shaded areas. Flowering begins about the fifthyear; a tree may annually yield up to 34 kg (75 pounds) of dried buds. The buds are hand-pickedin late summer and again in winter and are then sun-dried. Cloves vary in length from about 13 to 19 mm (0.5 to 0.75 inch).

The buds contain 14 to 20 percent essential oil, the principal component of which is the aromatic oil eugenol. Cloves are strongly pungent owing to eugenol, which is extracted by distillation to yield oil of cloves. This oil is used to prepare microscopic slides for viewing and is also a local anaesthetic for toothaches. Eugenol is used in germicides, perfumes, and mouthwashes, in the synthesis of vanillin, and as a sweetener or intensifier.

ECOLOGY

The word clove, first used in English in the 15th century, derives via Middle English clow of golfer, Anglo-French Clowes de gilofre and Old French clou de girofle, from the Latin word clavus "nail". The related English word gillyflower, originally meaning "clove", derives via said Old French girofle and Latin caryophyllon, from the Greek caryophyllene "clove", literally "nut leaf".

The use of clove for any medicinal purpose has not been approved by the US Food and

Drug Administration, and its use may cause adverse effects if taken orally by people with liver disease, blood clotting and immune system disorders, or food allergies.

Cloves are used in traditional medicine as an essential oil, which is used as an anodyne (analgesic) mainly for dental emergencies and other disorders. There is evidence that clove oil containing eugenol is effective for toothache pain and other types of pain, and onereview reported the efficacy of eugenol combined with ZnO as an analgesic. Clove essential oil may prevent the growth of Enterococcus faecalis bacteria which is often present in a root canal treatment failure.

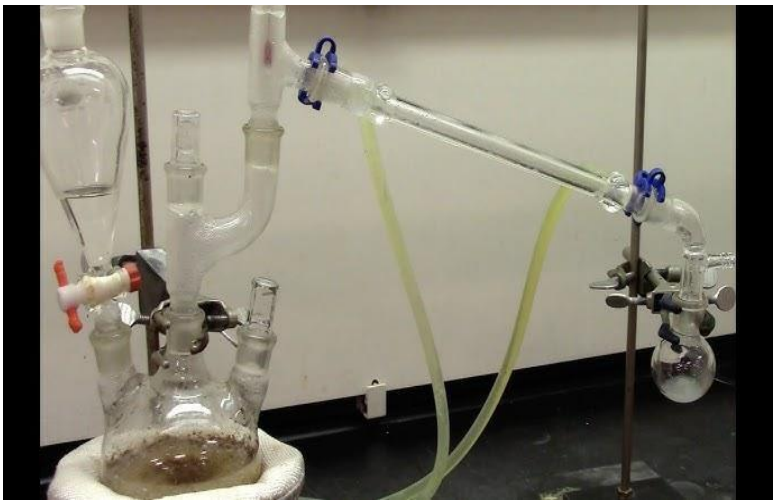
CULTIVATION

Here are some tips for cultivating Clove:

- **Soil:** Clove trees grow best in deep, rich, loamy soils with high humus content.
- **Climate**: Clove trees prefer a humid tropical climate with an annual rainfall of 150–250 cm and a mean temperature range of 20–30°C. They can tolerate short periods below 10°C, but temperatures below 5°C can damage the tree.
- **Sunlight:** Clove trees prefer partial shade.
- **Watering:** Clove trees need a constant supply of water, especially during the first three to four years of their life. Use a drip irrigation system to avoid waterlogging or root rot.
- **Fertilizing:** Apply a moderate amount of fertilizer once or twice a year, with the first dose in the spring.
- **Planting:** Collect seeds from fully developed fruits, known as the "mother of clove". Sow the seeds flat at a depth of 2–5 cm and a spacing of 12–15 cm. Transplant two-year-old seedlings into pits that are 30 cm x 30 cm x 30 cm in size.
- **Intercropping:** Clove trees can be intercropped with banana to create a cool, humid microclimate. They can also be mixed cropped with coconut or areca nut plantations, or in coffee estates.

Figure5: Cultivation of clove

EXTRACTION



Soxhlet Unit Extracting Clove Oil

Clove represents one of the major vegetal sources of phenolic compounds as flavonoids, hydroxybenzoic acids, hydroxycinnamic acids and hydroxyphenyl propene. Eugenol is main bioactive compound of clove, which is found in concentrations ranging from 9381.70 to 14
650.00 mg per 100 g of fresh plant material.
With regard to the phenolic acids, gallic acid is the compound found in higher concentration (783.50 mg/100g fresh weight). However, other gallic acid derivates as

hydrolysable tannins are present in higher concentrations (2 375.8 mg/100 g). Other phenolic acids found in clove are

the caffeic, ferulic, ellagic and salicylic acids. Flavonoids as kaempferol, quercetin and its derivates (glycosylated) are also found in clove in lower concentrations.

Concentrations up to 18% of essential oil can be found in the clove flower buds. Roughly, 89% of the clove essential oil is eugenol and 5% to 15% is eugenol acetate and β-cariofileno. Another important compound found in the essential oil of clove in concentrations up to 2.1% is α- humulenes. Other volatile compounds present in lower concentrations in clove essential oil are β-pinene, limonene, farnesol, benzaldehyde, 2-heptanone and ethyl hexanoate.

PHYTOCHEMICAL TEST

Estimation of Total Poly Phenols:

The total polyphenolic content (TPC) was determined by using the Folin-Ciocalteu method with slight modifications. 1:10 Follin-Ciocalteau reagent was mixed with 7% sodium carbonate. Gallic acid was used for preparation of the standard curve. The colorimetric change was measured in a UV-VIS spectrophotometer, and the absorbance read at 765 nm. Concentration ofthe total polyphenol content was expressed as mg Gallic acid equivalent/cup of tea.

Estimation of Total Flavonoids:

Total flavonoid content (TFC) was estimated by the aluminium chloride colorimetric assay with slight modifications. 5% Sodium nitrate were mixed with 10% Aluminium chloride. After 6 mins 1M Sodium hydroxide was added. Catechin was used as the standard for preparing the calibration curve. The colorimetric change was measured in a UV-VIS spectrophotometer, and the absorbance read at 510 nm. Concentration of the total flavonoid was expressed as mg Catechin equivalent/cup of tea.

DPPH Radical Scavenging Assay:

The free radical scavenging assay was performed according to the standard method (Shen et al. 2010) with a slight modification by using Ascorbic acid as standard. The colorimetric change was measured in a UV-VIS spectrophotometer, and the absorbance read at 517 nm against methanol used as blank. The DPPH radical scavenging activity was expressed in terms of Ascorbic acid equivalent, and the percentage of inhibition calculated by the following formula:

% Inhibition of DPPH = [(Absorbance of control –Absorbance of the sample)/ Absorbance of control] *100.

ADVERSE EFFECT

Even small amounts of clove oil can cause severe side effects such as seizures, liver damage, and fluid imbalances. Bleeding disorders: Clove oil contains a chemical called eugenol that seems to slow blood clotting. Taking clove oil might cause bleeding in people with bleeding disorders.

When taken by mouth: Clove is commonly consumed in foods. There isn't enough reliable information to know if taking clove in larger amounts is safe or what the side effects might be.

When applied to the skin: Clove oil or cream containing clove flower is possibly safe. But applying clove oil in the mouth or on the gums can sometimes cause irritation and gum damage. Applying clove oil or cream to the skin can sometimes cause burning and skin irritation.

When inhaled: Smoke from clove cigarettes is likely unsafe and can cause side effects such as breathing problems and lung disease.

HEALTH BENEFITS OF CLOVE

The main health benefits of cloves include:

- Fighting infections.
- Preventing cancer.
- Decreasing pain.
- Repelling mosquitos and other insects.
- Boosting libido.
- Treating bad breath.
- Promoting optimal digestion.
- Speeding-up wound healing.

MECHANISM OF ACTION

The exact mechanism of action of eugenol is unknown. However, eugenol has been shown

to interrupt action potentials, which may be involved in its anti-pain activity. Research has also shown eugenol to have anti-inflammatory, neuroprotective, antipyretic, antioxidant, antifungal and analgesic properties.

Pharmacologically, clove and its main constituents possess antimicrobial, antioxidant, anti-inflammatory, analgesic, anticancer, and anesthetic effects. Moreover, they showed insecticidal, mosquito repellant, aphrodisiac, and antipyretic activities.

Cloves contain a lot of manganese, a mineral that helps your body manage the enzymes that help repair your bones and make hormones. Manganese can also act as an antioxidant that protects your body from harmful free radicals (unstable atoms that cause cell damage). Cloves are also a great source of: Vitamin K.

Its dried flower buds are a popular spice and are also used in Chinese and Ayurvedic medicine. Clove oils, dried flower buds, leaves, and stems are used to make medicine. Clove oil contains a chemical called eugenol that might help decrease pain and fight infections. Clove is also a popular ingredient in cigarettes.

- **Blocking acetylcholine:**

  Eugenol, the main component of clove oil, may block the neuromuscular transmitter substance, acetylcholine.

- **Antagonizing vanilloid receptors:**

  Eugenol may have analgesic properties by antagonizing the vanilloid receptor and transient receptor potential vanilloid.

- **Modulating GABA receptors:**

  Clove oil may modulate the binding of muscimol to GABA receptors.

CONTRAINDICATIONS

Taking clove oil might cause bleeding in people with bleeding disorders. Surgery: Cloves contain chemicals that might affect blood sugar levels and slow blood clotting. It might interfere with blood sugar control or cause bleeding during or after surgery. Stop using clove at least 2 weeks before a scheduled surgery.

Cloves are contraindicated for use by pregnant or breastfeeding women, and by children under 6 years old, as there are no studies to guarantee its safety. It is also not

recommended for people with a history of gastritis or ulcers.

Cloves can cause skin irritation and digestive tract irritation in some people; therefore, it should be used as directed by a doctor or medicinal plant specialist.

Furthermore, eugenol, which is one of the components of cloves, can be toxic when consumed in its pure form and in large quantities (with concentration greater than 600 mg/mL).

Cloves can also interact with some medications, such as antidiabetics and anticoagulants, and it is important to consult your doctor before consuming cloves.

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