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## A review on therapeutic potential of *Digitalis purpurea* L. in perspective of Unani medicine

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**Abstract**

*Digitalis purpurea* L. (foxglove) is an important medicinal plant belonging to the Scrophulariaceae family. It is native to northern Africa (i.e., Morocco) and Europe (i.e. Denmark, France, Portugal, Norway, Sweden, the UK, Germany, Italy, and Spain). Its leaves have cardio-tonic, diuretic, sedative, hemostatic, antipyretic properties etc., and are used for the treatment of left ventricular hypertrophy of the heart, palpitations, ascites, epistaxis, hemoptysis, menorrhagia, epilepsy, pneumonia, chronic pleurisy, wounds, and burns. A variety of phytoconstituents are isolated from *Digitalis*, which include glycosides, saponins, flavonoids, organic acids, tannins, mucilage etc. Various pharmacological studies on the plant have been done, like cardiovascular, hepatoprotective, antidiabetic, insecticidal, antioxidant, etc. The aim of the paper is to highlight the therapeutic applications as described in Unani literature and scientific studies done on *Digitalis purpurea*.

**Keywords:** *Digitalis purpurea*, foxglove, Muqawwi-i-Qalb, cardiovascular diseases, digoxin, unani medicine

**Introduction**

*Digitalis purpurea* is a member of the Scrophulariaceae family [1]. There are mainly two species, namely *Digitalis lanata* L. and *Digitalis purpurea* L., which are used medicinally [2]. Primarily, Dr. Blorindi (1721) and then Dr. Mori (1788) mentioned this plant in *Pharmacopoea* [3]. *Digitalis purpurea* is native to the British-isles, temperate Western Europe, and Morocco. It is commercially cultivated as a drug plant in Austria, England, Germany, Hungary, Japan, and India [4]. In Kashmir, it has been cultivated at an altitude of 7000 feet in the Kiro forests at Tang Marg, it is also found in the Himalayas at an altitude of 7000-10,000 feet [5]. It is commonly known as digitalis, while in English it is also called foxglove or purple foxglove [6]. This is a biennial herb with an erect stem that attains a height of 1.5m. Leaves are ovate and hairy, which produces a rosette of basal leaves. The lower basal leaves are long-stalked, while the upper leaves are almost without stalks. Flowers appear in erect, showy, usually one-sided spikes, white or purple in colour with ciliate lobes. The fruit is a capsule, the style persists on the top of the fruit after flowering [1, 4]. Congestive cardiac failure and arrhythmias are two ailments for which *D. purpurea* is well-known to be quite beneficial. It has several steroidal and cardiac glycosides that are concentrated in the leaves and roots [7]. Among its active ingredients, the well-known glycosides are Digitoxin, Jaitoxin, and Jatitalin. The glycoside is primarily used in the treatment of heart diseases. It aids in relieving the heart and energising the heart muscle tissue. In the event of blocked heart arteries, it increases the blood flow to the coronary arteries, facilitating heart growth. The seeds contain a thick vegetable oil with a distinctive flavour, and the leaves are fragrant. Dried leaves are used for creating fragrances [10].

**Materials and Methods**

All available classical text books were searched for the literature review with the key words *Digitalis purpurea*, foxglove, and *Muqawwi-i-Qalb* in Unani medicine. Additionally, Google Scholar, Research Gate, and PubMed were also searched using the keyword's *Digitalis purpurea*, Foxglove, etc. Review articles, clinical trials, and experimental studies were taken into consideration for data generation and analysis.

**Geographical Distribution:** The species is native to the British Isles, temperate western Europe, and Morocco. It is commercially cultivated as a drug plant in Austria, England,

Germany, Hungary, and Japan. In India, it is cultivated in Kashmir, Darjeeling, and Nilgiri Hills [4].

### Botanical description

The pubescent plant is a biennial with a branched tap root system. The plant produces a leaf rosette during the first year (Fig. 1a), and a 2m tall, straight, unbranched, grey, tomentose stem is produced in the second year. The leaves are oval, alternating, petiolate, and tapering upward (Fig. 1b). The majority of the leaves are crenate; only the topmost ones have full margins. The flowers have white dots on the sides and a

carmine crimson colour. Long terminal mono-side racemes with flowers on them are the common form; they possess five free sepals with short tips (Fig. 1d and e). The corolla is campanulate, bilabiate, and about 4 cm long; the lower lip has an elliptical apex, while the upper lip is obtuse (Fig. 1d). These consist of one superior ovary, two long stamens, and two short stamens. The fruit is an oval, glandular, villous capsule ((Fig. 1f) with two valves [7]. Seeds are small, light, and numerous (Fig. 1g). They contain digitalin and also yield a fatty oil. [8, 9].



**Fig 1:** Plant with a leaf rosette during the first year and dorsal of leaf (a & b), flowering in *Digitalis lanata* and *Digitalis purpurea* (c & d), stem, flowers, fruits (c, d, e & f) and seeds of *Digitalis purpurea* (g).

**Cultivation and Collection:** As the seeds of *Digitalis* are small (Fig. 1.g), they are sown by mixing them with fine sand to ensure even distribution and sown in prepared nursery beds in March or April. When 2/3 of the flowers are fully mature, leaves are harvested. After that, the seedling is placed in the field. In the early afternoon, leaves are typically picked because it is thought that this is when the most cardio-active glycosides are present. After being collected below 60°C, the leaves are quickly dried, and the dried leaves are kept in a sealed container. Because excessive moisture promotes the hydrolysis of cardiac glycosides, which lowers cardiac activity, dried leaves should not contain more than 5% moisture [11]. The leaves are collected in early the mornings and dried in shade. They contain digitalin and digoxin in very small quantities [12].

### Habitat

Woodlands, forest clearings, grasslands, slopes, preferring moist situations [12].

### Taxonomical Classification:

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnolipsida

Order: Scrophulariales

Family: Scrophulariaceae

Genus: *Digitalis*

Species: *Digitalis purpurea* L.

**Description in Unani literature:** *Digitalis* is a small plant, 3 or 4 feet tall; leaves are plucked only when they are dried and when the plant is about 2 years old. The leaves are about 4-12 inches long or more and 5-6 inches broad, ovate, lobed, and irregularly saw-toothed. The upper surface of the leaves is green with slight glandular hairs, and the lower surface is yellowish with abundant glandular hairs. The taste is very unpleasant, but the smell is pleasant, just like the smell of tea. [3].

### Mutarādīfāt (Vernacular names)

English: Foxglove or purple Foxglove, *Digitalis purpurea* [4, 5].

Ayurvedic: Hritpatri, Tilapushpi [6]

Sanskrit: Tilapuspi (yellow flower variety) [13]

Tamil: Nilapukaiyilai (Purple flower variety) <sup>[13]</sup>

**Ajza-i-Musta'mala (Parts used):** Leaves <sup>[13]</sup>

**Mizāj (Temperament):** hot and dry (according to its actions)

**Miqdār Khūrāk (Dose):** 31.25 mg -93.75 mg, Tincture (10 drops-30 drops) of Digitalinum <sup>[3]</sup>.

**Af'al (Action):** It has *Mudir-i-Hayd* (emmenagogue), *Mudir-i-Bawl* (diuretic), *Musakkin* (sedative), *Muqawwi-i-Qalb* (cardio tonic), *Hābis-i-Khūn* (haemostatic), Vasculo-stimulant, negative chronotropic, positive inotropic action. Digitalis glycosides increase the force of contraction of the heart without increasing oxygen consumption and slow the heart when auricular fibrillation is present <sup>[3, 6, 14]</sup>.

**Iste'mālāt (therapeutic uses):** It is used for the treatment of cardiovascular disease, *Khafaqān* (palpitation), *Istisqā* (Ascites), *Izām al-Qalb* (Hypertrophy of heart), Carotid artery stenosis, *Fever*, *Naksīr* (epistaxis), *Nafth al-Dam* (haemoptysis), *Istihāda* (menorrhagia), *Sar'* (epilepsy), *Dhāt al-Ri'a* (pneumonia), *Dhāt al-Janb Muzmin* (chronic pleurisy), Oedema, *Ikhtilāj-i-Qalb* (cardiac fasciculation) <sup>[3]</sup>, congestive heart failure, wound healing, burns, asthma, heart failure <sup>[4, 13]</sup> etc.

**Maqarrat (toxicity, side effects and adverse effects):** The glycosides (Digoxin) are dangerous in high doses, and they tend to accumulate in the body and cause poisoning. The symptoms of poisoning include abdominal pain, irritation of the stomach and bowel, nausea, vomiting, weakness, an irregular and feeble pulse, dilatation of the pupil, cold sweating, anuria, syncope, abnormal heart action, and perhaps tremors and convulsions <sup>[1, 3]</sup>.

**Note:** Digitalis should be used only under strict medical supervision.

**Badal (substitutes):** Leaves of other species of *Digitalis* are used as substitutes <sup>[15]</sup>.

**Adulteration:** The more common adulterants of the drug, especially of the crushed form, are the leaves of *Verbascum thapsus* L., *Symphytum officinale* L., and *Inula* spp. The presence of adulterants can be detected by microscopic examination <sup>[15]</sup>.

#### **Tarkīb Iste'māl (mode of administration)**

- Infusions of Digitalis leaves are used to relieve sore throats and asthma <sup>[4]</sup>.
- An ointment containing digitalis glycosides is used for wound healing and burns <sup>[4]</sup>.
- *Khīshānda* (infusion) of Digitalis is used as cardio-tonic and diuretic <sup>[3]</sup>.

**Chemical Constituents:** Cardiac glycosides, digitoxin, gotoxin, gitaloxin, strospeside, phenolic glycosides, desrhamnosyl acetoside, and purpureosides A and B are present in the plant <sup>[13]</sup>. The leaves contain at least 30 glycosides, K, Ca, and flavonoids; leaves and seeds contain several saponins like digitonin, gitonin, and tigonin, seeds also contain digitalin <sup>[1, 4]</sup>. The leaf-stalk contains febrifugine and an enzyme that catalyses the conversion of progesterone to beta-pregnane-3,20-dione. Four phenolic glycosides were isolated from the leaf and stem callus tissues and identified as purpureasides A, and B: acetoside, 3,4-dihydroxy-phenethyl-

alcohol-6-O-beta-D-galatopyranosyl-4-O-caffeoyl-beta-D-glucoside <sup>[16]</sup>.

**Glycoside levels:** highest in June-August, lowest in December <sup>[1]</sup>.

#### **Pharmacological studies**

**Cardiovascular activity and mechanism:** A glycoside extracted from *Digitalis purpurea* was tested for its emetic effect in pigeons, urinary excretion in rats, and isolated cardiac arrhythmias in rabbits. In a dose-dependent manner, the methanolic extract increased the auricle's contraction force at doses of 20 and 40 mg/ml. A mild diuretic and natriuretic effect is noted at doses of 15 and 30 mg/kg. The emesis active dose range was 0.5-4 mg/kg, and it was noted that the emesis time decreased in a dose-dependent manner within 10 minutes of injection <sup>[17]</sup>. Digitalis glycosides compete with potassium for binding to potassium ATPase (Na<sup>+</sup>/K<sup>+</sup>-ATPase) and also prevent potassium from binding to this enzyme. The heart contracts more forcefully than normal because the heart muscle is exposed to calcium for a longer period of time than usual. Ion pumping and the more recently identified signal-transducing function of Na<sup>+</sup>/K<sup>+</sup>-ATPase are the two mechanisms through which digitalis glycosides affect the heart. Many growth-related signal transduction pathways are activated as a result of this enzyme's participation in protein-protein interactions. Some of these pathways play an important role in the enhanced contractibility of the heart that is induced by digitalis. <sup>[18, 19, 20]</sup>.

**Hepatoprotective activity:** The hepatoprotective efficacy of *Digitalis purpurea* methanolic extract in albino rats exposed to CCl<sub>4</sub>-induced hepatotoxicity was assessed. Serum levels of total bilirubin, alkaline phosphatase (ALP), aspartate aminotransferase (SGOT), and alanine aminotransferase (SGPT) were measured to assess hepatotoxicity. Elevated serum levels of SGOT, SGPT, ALP, and total bilirubin indicated that rats receiving CCl<sub>4</sub> had serious liver damage. In both preventive and curative models, the extract of *Digitalis purpurea* and silymarin administration inhibit the toxic effect of CCl<sub>4</sub> on the above-mentioned serum parameters <sup>[21]</sup>.

#### **Digitalis and other drugs that reduce mortality in heart failure:**

Before beta blockers and angiotensin receptor blockers (ARB's) studies, consider using digitalis and other medications that lower mortality. It has been demonstrated that ACE inhibitors, when used with diuretics and digitalis increases survival <sup>[22-24]</sup>. Furthermore, it has been demonstrated that spironolactone and beta blockers increase survival rates when combined with ACE inhibitors, digitalis, and diuretics <sup>[25]</sup>. But it's unclear how beneficial they are <sup>[26]</sup>. In addition to medication therapy, implanted cardioverter-defibrillators (ICD's) and cardiac resynchronization therapy (CRT) have increased the survival rate of heart failure patients.

#### **Conclusion**

Reading about the *Digitalis purpurea* in various books, it has been revealed that it has several applications for treating a range of illnesses, especially cardio-vascular diseases like palpitations, ascitis, hypertrophy of the heart, epistaxis, hemoptysis, menorrhagia, epilepsy, pneumonia, chronic pleurisy, cardiac fasciculations, etc. Hence, this review will help to conduct scientific studies on the unexploited potential of this plant to get the maximum benefits.

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**Conflicts of Interest:** Nil

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