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DIGITALIS PURPUREA: AN OVERVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL PROFILE

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ABSTRACT: *Digitalis purpurea* commonly known as foxgloves belong to the genus *Digitalis*, which is a member of the family Plantaginaceae. Due to their effectivity in the treatment of heart insufficiency, cardenolides from *Digitalis* have been used extensively worldwide. *Digitalis purpurea* is the most important source of cardiac glycosides or cardenolides, volatile oil, fatty matter, starch, gum, and sugars. They possessed cardiovascular, cytotoxic, anti-diabetic, antioxidant, insecticidal, immunological, hepatoprotective, neuro-protective and cardioprotective effects. This review highlights the plant profile, history, chemical constituents, chemical test, traditional uses, drug interaction and pharmacological effects of *Digitalis purpurea*.

INTRODUCTION: The plants provided food, clothing, shelter, and medicine. As time went on, each tribe added the medicinal power of herbs in their area to its knowledge base [1]. Seventy-five percent of the world's population used plants for therapy and prevention [1]. However, plants are a valuable source of a wide range of secondary metabolites, which are used as pharmaceuticals, agrochemicals, flavors, fragrances, colors, bio-pesticides and food additives [2, 3]. *D. purpurea* was named by the Swedish botanist Carl Linnaeus in his pivotal publication species Plantarum in 1753. The generic name Digitalis comes from the Latin for finger (digitus), referring to the shape of the flowers. The specific epithet purpurea refers to the color of the flowers, which are frequently purple (although a white-flowered form is fairly common).

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Common foxglove is a popular ornamental, and many hybrids and cultivars are available [4]. The physician/scientist credited with bringing *Digitalis* into mainstream medicine is William Withering. Foxglove had already been in use as a traditional herbal remedy for "dropsy," the swelling that often accompanies heart failure [5]. In the 1780s, Withering observed the remarkable effectiveness of *Digitalis*/foxglove in a woman who had dropsy, and he began a rigorous study of the drug. *Digitalis* is a drug that has been used for centuries to treat heart disease. The other uses of digitalis include asthma, epilepsy, tuberculosis, constipation, headache, spasm, wounds, and burns, causing vomiting and other conditions.

The plant's name, *Digitalis* (from the Latin digit, finger) describes the finger-shaped purple flowers it bears. The tall flower spikes with charming tubular flowers of foxglove add both height and vertical accent to your garden without staking. Perennial *Digitalis* blooms attract hummingbirds and bees and a bonus, the deer do not like the foliage [6]. *Digitalis purpurea* contains cardiac glycosides, volatile oil, fatty matter, starch, gum and sugars.

They possessed cardiovascular, cytotoxic, anti-diabetic, antioxidant, insecticidal, immunological, hepatic, neuro and cardioprotective effects.

Plant Profile:

Taxonomic Classification of *D. purpurea* Plant:

Kingdom	: Plantae
Subkingdom	: Viridiplantae
Infrakingdom	: Streptophyta
Superdivision	: Embryophyta
Division	: Tracheophyta
Subdivision	: Spermatophytina
Class	: Magnoliopsida
Superorder	: Asteranae
Order	: Lamiales
Family	: Plantaginaceae
Genus	: Digitalis
Species	: *D. purpurea* [7, 8]

Botanical Description: It is a biennial or perennial herb. It is about 1 to 2 meters in height. Flower and Fruit: The flowers are carmine red with white edged spots on the inside. The flowers appear in long hanging racemes. They have 5 free, short-tipped sepals. The corolla is about 4 cm long, campanulate, bilabiate with an obtuse upper lip and an ovate tip on the lower lip. The flower is glabrous on the outside and has a white pawn on the inside. There are 2 long and 2 short stamens, and 1 superior ovary. The fruit is a 2-valved, ovate, glandular, villous capsule.

The plant with a branched taproot. In the first year, it develops a leaf rosette. In the second it produces a 2 m high, erect, unbranched, gray, tomentose stem. The leaves are alternate, ovate, tapering upward and petiolate. Almost all leaves are crenate; only the highest ones are entire-margined [9, 10].

FIG. 1: *DIGITALIS PURPUREA* LINN. PLANT

Synonym: Arabic: Asabi athara hamra, kafaz elthalab, digital erjwani, kameiat riz; Ayurvedic: Hritpatri, Tilapushpi; Chinese: mao di huang; English: purple foxglove, digitalis, foxglove, common foxglove, fairy fingers, fairy gloves; Korean: digitalriseu; Swedish: fingerborgsblomma.

Biological Source: *Digitalis* consists of dried leaves of *Digitalis purpurea* Linn., family-Scrophulariaceae. After collection leaves are dried immediately at a temperature below 60 ºC and they contain no more than 5% moisture. After drying leaves are stored in moisture-proof container.

Geographical Distribution: *Digitalis purpurea* is thought to be native to West, South-West and West Central Europe. It is distributed in Africa (Morocco, Cape Verde, Madeira Islands, Canary Islands), Europe (Belgium, Germany, Finland, Ireland, Norway, Sweden, United Kingdom, Albania, Italy, France, Portugal, Spain, Czech Republic, Denmark, and Croatia) [12, 13]. It is found in European countries, England, France, Germany, North America, and India. In India, it is cultivated in Kashmir and Nilgiri Hill [14].

Cultivation and Collection: The seed of digitalis are small in size, so they are mixed with sand for sowing. Leaves are collected in both the years but leaves collected when 2/3 of flowers are fully developed. The seedling is then transplanted into the field. Generally, the leaves are collected in the early afternoon, with the belief that maximum cardio-active glycosides are present at that time. The leaves are immediately dried after collection

below 60 ºC and dried leaves are stored in airtight containers. The dried leaves should not contain more than 5% moisture since it promotes hydrolysis of cardiac glycosides resulting in loss of cardiac activity [15].

Organoleptic Characters:

General Appearance: Usually broken and crimped.

Shape: Ovate-lanceolate.

Size: 10 to 40 cm long and 4 to 10 cm.

Wide Margin: Crenate or dentate.

Apex: obtuse or rounded.

Base: Tapering, decurrent.

Upper Surface: Slight pubescent, dark green, little wrinkled, one water pore present near each tooth

Lower surface: Grayish-green, very pubescent

Venation: Pinnate, mid-rib, lateral vein, veinlet, and still smaller vein let prominent on the under-surface; lateral vein leaves the midrib, at an acute angle and anatomies on the margin.

Petiole: Winged, 2.5 to 10 cm long [16].

Adulterants:

Primrose Leaves: Leaves of *Primula vulgaris* Huds (Fam: Pimulaceae).

Comfrey Leaves: Leaves of *Symphytum officinale* Linn. (Fam: Boraginaceae).

Mullein Leaves: Leaves of *Verbascum thapsus* Linn. (Fam: Scrophulariaceae).

Preparations:

1. Specific medicine digitalis. Dose, 1/5 to 1 drop.
2. *Infusum digitalis*. Infusion of Digitalis. (A cinnamon-flavored, 1 1/2 percent, infusion). Dose, 1 to 2 fluidrachms.
3. *Tinctura digitalis*, tincture of *Digitalis* (10 percent of the drug). Dose, 1 to 10 drops.

Dosage: *Digitalis* leaf provides a narrow therapeutic index, requiring close medical supervision for safe use. Classical dosage started at 1.5 g of a leaf divided between 2 daily doses. Purified digoxin is typically used at daily doses of 0.125 to 0.25 mg.

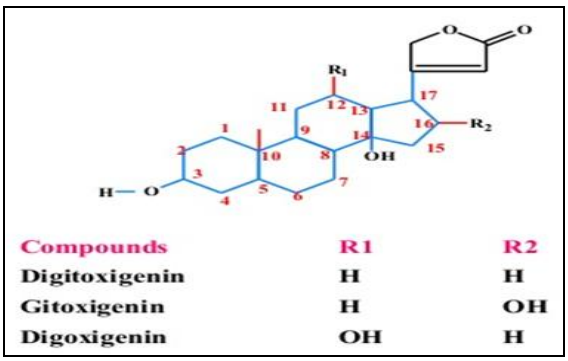
Traditional Uses: Earlier, *Digitalis species* were used to treat ulcers, boils, abscesses, headaches, and paralysis. Externally, digitalis species were used for the granulation of poorly healing wounds and to cure ulcers. After William Withering work, the digoxin is isolated from *Digitalis species* as a life-saving cardiac drug. *Digitalis* has long been used as a treatment for heart failure in addition to a range of other traditional uses.

The plant is cultivated as an ornamental [14]. Foxglove is used for congestive heart failure (CHF) and relieving associated fluid retention (edema), irregular heartbeat, including atrial fibrillation and flutter. Also used in asthma, epilepsy, tuberculosis; constipation; headache; and spasm. It is also used to cause vomiting and for healing wounds and burns [11, 14].

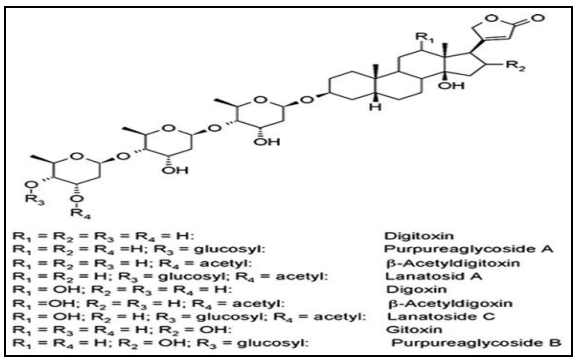
Chemical Profile:

Plant *Digitalis purpurea* Contained:

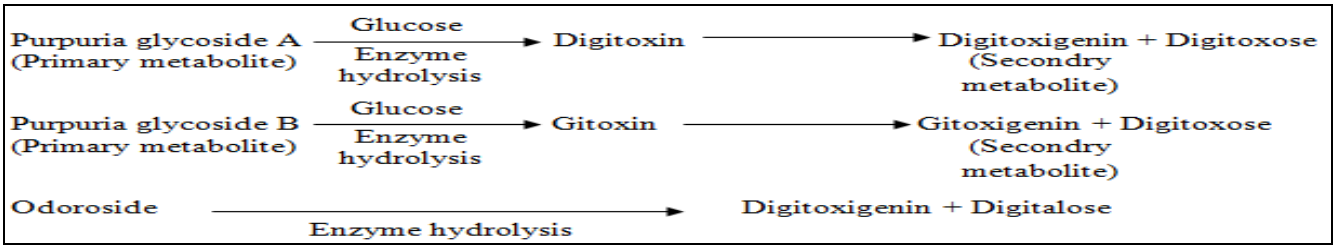
Cardioactive Steroid Glycosides: (cardenolides 0.5 to 1.5%) including [Aglycone digitoxigenin: purpurea glycoside A (primary glycoside), digitoxin (secondary glycoside)]; [Aglycone gitoxigenin: purpurea glycoside B (primary glycoside), gitoxin (secondary glycoside)]; [Aglycone gitaloxigenin: glucoverodoxin, glucogitaloxin, gitaloxin]; [Preg-nane glycosides: including digipurpurin, diginin, digitalonin].

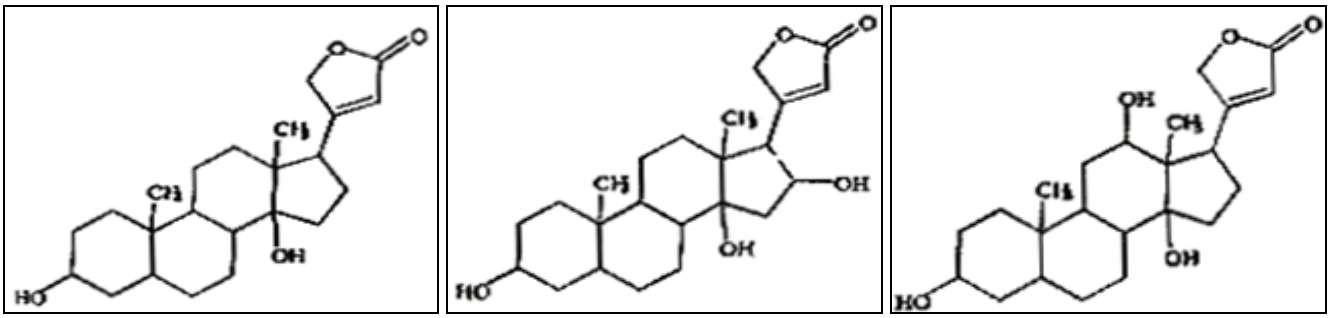


Compounds	R1	R2
Digitoxigenin	H	H
Gitoxigenin	H	OH
Digoxigenin	OH	H



$R_1 = R_2 = R_3 = R_4 = H$:	Digitoxin
$R_1 = R_2 = R_4 = H$; R_3 = glucosyl:	Purpureaglycoside A
$R_1 = R_2 = R_3 = H$; R_4 = acetyl:	β-Acetyldigitoxin
$R_1 = R_2 = H$; R_3 = glucosyl; R_4 = acetyl:	Lanatosid A
R_1 = OH; $R_2 = R_3 = R_4 = H$:	Digoxin
R_1 =OH; $R_2 = R_3 = H$; R_4 = acetyl:	β-Acetyldigoxin
R_1 = OH; $R_2 = H$; R_3 = glucosyl; R_4 = acetyl:	Lanatoside C
$R_1 = R_3 = R_4 = H$; R_2 = OH:	Gitoxin
$R_1 = R_4 = H$; R_2 = OH; R_3 = glucosyl:	Purpureaglycoside B





Digitoxigenin **Gitoxigenin** **Digoxigenin**

FIG. 2: CHEMICAL CONSTITUENTS OF *DIGITALIS PURPUREA*

Steroid Saponin: Including desgalactotigonin. digitonine, purpureagitoside.

Anthracene Derivatives: Anthraquinones [17].

Four different glycosides including acteoside, purpureaside A, calceolarioside B, and plantain side D were isolated from the leaves of *Digitalis purpurea* [18].

The Minerals: Boron (B), chromium (Cr), manganese (Mn), cobalt (Co), nickel (Ni), copper (Cu), arsenic (As) and lead (Pb), in various plant parts of *Digitalis purpurea* at pre and post-flowering stages were determined. The concentration of most of the minerals was higher at post flowering than that of pre-flowering stage [19].

Chemical Tests:

Raymond's Test: To the drug, add a few ml of 50% ethanol and 0.1 ml of 1% solution of m-dinitrobenzene in ethanol. To this solution, add 2-3 drops of 20% sodium hydroxide solution. Violet coolers appear, this is due to the presence of an active methylene group.

Legal Test: To the drug, add a few ml of pyridine and 2 drops of nitroprusside and a drop of 20% sodium hydroxide solution. A deep red color is produced.

Killer Killiani Test: Glycoside is dissolved in a mixture of 1% ferric sulfate solution in (5%) glacial acetic acid. Add one or two drops of concentrated sulphuric acid. A blue color develops due to the presence of deoxy sugar.

Xanthydrol Test: The crude is heated with 0.1 to 5% solution of xanthydrol in glacial acetic acid containing 1% hydrochloric acid. Red color is produced due to the presence of 2-deoxysugar.

Baljet Test: Take a piece of lamina or thick section of the leaf and add sodium picrate reagent. If glycoside is present yellow to orange color will be seen [20].

Pathophysiology: Digoxin's inotropic effect results from the inhibition of the sodium-potassium adenosine triphosphatase (Na^+ /K^+ATPase) pump. The subsequent rise in intracellular calcium (Ca^{++}) and sodium (Na^+) coupled with the loss of intracellular potassium (K^+) increases the force of myocardial muscle contraction (contractility), resulting in a net positive inotropic effect. Digoxin also increases the automaticity of Purkinje fibers but slows conduction through the atrioventricular (AV) node. Cardiac dysrhythmias associated with an increase in automaticity and a decrease in conduction may result. The relationship between digoxin toxicity and the serum digoxin level is complex; clinical toxicity results from the interactions between digitalis, various electrolyte abnormalities, and their combined effect on the Na^+ /K^+ ATPase pump. Cardiac, such as oleander, foxglove, and lily-of-the-valley, is uncommon but potentially lethal. Case reports of toxicity from

these sources implicate the preparation of extracts and teas as the usual culprit [21].

Drug Interaction: Drug interactions are one of the most common causes of digoxin toxicity. Some medications directly increase digoxin plasma levels; other medications alter renal excretion or induce electrolyte abnormalities. Drugs that have been reported to cause digoxin toxicity include the following:

- Amiloride, - May, reduce the inotropic response to digoxin.
- Amiodarone - Reduces renal and nonrenal clearance of digoxin and may have additive effects on the heart rate.
- Benzodiazepines (alprazolam, diazepam) - Have been associated with isolated reports of digoxin toxicity.
- Beta-blockers (propranolol, metoprolol, atenolol) - May have additive effects on the heart rate; carvedilol may increase digoxin blood levels in addition to potentiating its effects on the heart rate.
- Calcium channel blockers - Diltiazem and verapamil increase serum digoxin levels; not all calcium channel blockers share this effect.
- Cyclosporine - May increase digoxin levels, possibly due to reduced renal excretion.
- Erythromycin, clarithromycin, and tetracyclines - May increase digoxin levels.
- Propafenone - Increases digoxin level; effects are variable.
- Quinidine - Increases digoxin level substantially but the clinical effect is variable; related drugs such as hydroxychloroquine or quinine may also affect levels.
- Propylthiouracil - May increase digoxin levels by reducing thyroid hormone levels.
- Indomethacin.
- Spironolactone, - May, interfere with digoxin assays; may directly increase digoxin levels; may alter renal excretion.
- Hydrochlorothiazide.
- Furosemide and other loop diuretics.
- Triamterene.
- Amphotericin B - May precipitate hypokalemia and subsequent digoxin toxicity.
- Succinylcholine - Increased risk of dysrhythmias has been reported.
- Herb/nutraceutical - Avoid ephedra (risk of cardiac stimulation); avoid natural licorice (causes sodium and water retention and increases potassium loss).
- Clinical digoxin toxicity represents a complex interaction between digoxin and various electrolyte and renal abnormalities. A patient with normal digoxin levels (0.5-2 ng/mL) but renal insufficiency or severe hypokalemia may have more serious cardiotoxicity than a patient with high digoxin levels and no renal or electrolyte disturbances.

Precautions: In therapeutic doses, digitalis usually produces mild toxic effects. The toxic effects include headache, fatigue, drowsiness, nausea, vomiting and blurred vision. It is, therefore, necessary to regulate the dose in such a manner to avoid such effects. The toxic effects mentioned should be watched carefully and the dose regulated accordingly.

Mechanism of Action:
Direct Action: *Digitalis* binds to the sodium pump 1 on the myocardial cell membrane and inhibits its function. This pump when inhibited causes a rise in the amount of sodium inside the heart cell, which then exchanges it for calcium through the cell membrane, as calcium rises inside the heart cell contractile mechanism becomes more optimal and stronger [22].

Indirect Action: Parasympathetic nerve activation results in sinus 6 nodes slowing and thus bradycardia. It also inhibits the atrioventricular node [23, 24].

Pharmacokinetics:
Half-life: 1.5 days

Excretion: 60% through kidneys, 30% by the liver.

Body weight is crucial in determining the loading dose, as in a small child with low skeletal muscle mass; less of the loading dose will bind to skeletal

muscles and will rather rise the blood digoxin level and cause toxicity.

Pharmacological Effects:

Cardiovascular Effects: Cardiac glycosides are often called digitalis or digitalis glycosides, in particular, digoxin and digitoxin, have been a cornerstone of the treatment of heart diseases for more than two centuries. However, the identification of angiotensin converting enzyme inhibitors, *β*-adrenergic blockers and angiotensin-receptor blockers has significantly reduced their clinical use. The cardiac glycosides are with low therapeutic index. They possessed many cardio-vascular effects by many mechanisms [25, 26, 27, 28].

Antitumor Activity: Recent research has shown the anticancer effects of digitalis compounds, suggesting their possible use in medical oncology *D. purpurea* were identified as having cytotoxic properties, including cytotoxic activity, and warrant further study. Another study was supportive of investigations showing that apoptosis induction is a major effect of digitalis on several types of tumor cells [9]. The report demonstrated the anticancer activity of *D. purpurea*. L. heywoodi on 3 human cancer cell lines. The results of one study revealed marked differences in cytotoxicity between the cardiac glycosides [29].

Cytotoxic Effects: Extracts of plant examined for anticancer activity in 10 human tumor cell lines. They produced cytotoxic effects, but the activity profiles were uncorrelated with those of the standard drugs, possibly indicating new pathways of drug-mediated cell death [30].

Hepatoprotective Effects: 4 different glycosides (acteoside, purpureaside A, calceolarioside B, and plantain side D) isolated from the leaves of *Digitalis purpurea* were studied for their abilities to induce glutathione S-transferase (GST) and their protective efficiencies against aflatoxin B1-induced cytotoxicity in H4IIE cells. Of these four glycosides, acteoside significantly inhibited the cytotoxicity induced by aflatoxin B1 (AFB1) and also selectively increased GST alpha protein levels. Reporter gene analysis using an antioxidant response element (ARE) containing construct and subcellular fractionation assays, revealed that GST alpha induction by acteoside might be associated with Nrf2/ARE activation [32].

Neuroprotective Effects: The neuroprotective action of cardiac glycoside neriifolin was evaluated in ischemic stroke. Neriifolin provided significant neuroprotection in a neonatal model of hypoxia/ ischemia and a middle cerebral artery occlusion model of transient focal ischemia [32].

Cardioprotective Effects: The heart-protective effects of ouabain against ischemia-reperfusion injury, through activation of the Na^+, K^+ - ATPase/c-Src receptor complex, was studied. In Langendorff-perfused rat hearts, a short (4 min) administration of ouabain 10 muM followed by an 8 min wash out before 30 min of global ischemia and reperfusion, improved cardiac function, decreased lactate dehydrogenase release and reduced infarct size by 40%. Western blot analysis revealed that ouabain activated the cardioprotective phospholipase C gamma1/protein kinase Cepsilon (PLC-gamma1 / PKCepsilon) pathway. Pre-treatment of the hearts with the Src kinase family inhibitor 4-amino-5-(4-chlorophenyl)- 7-(t-butyl) pyrazolol[3,4-d]pyrimidine (PP2) blocked not only ouabain-induced activation of PLCgamma1/ PKCepsilon pathway but also cardiac protection. The protection was also blocked by a PKCepsilon translocation inhibitor peptide (PKCepsilon TIP) [33].

Antidiabetic Effect: Digitonin, a saponin from the seeds of *Digitalis purpurea*, improved glucose tolerance and possessed beneficial effects on serum lipids by improve antioxidant activity in rats [34].

Antioxidant Effect: The scavenging activity of alcoholic extract of *Digitalis purpurea* was measured using DPPH and the total antioxidant capacity of *D. purpurea* was measured by phosphomolybdate using ascorbic acid as the standard. *Digitalis purpurea* 1 mg/ml showed 94.25% DPPH scavenging activity and 92.28% total anti-oxidant activity [35].

Insecticidal Effect: Studying of insecticidal activity of alcoholic extract of *Digitalis purpurea* against *T. castaneum* revealed that the percentage mortality of *T. castaneum* was 60%, at 100 mg / 2ml of alcoholic extract of *Digitalis purpurea* [35].

Adverse Effects and Toxicity: Digitalis is a toxic plant. At low serum drug concentrations, digitalis was well tolerated. However, it characterized by a very narrow therapeutic index, and digitalis toxicity

was one of the most common adverse drug reactions leading to hospitalization. Anorexia, nausea, and vomiting may be initial indicators of toxicity. Patients may also experience blurred vision, yellowish vision (xanthopsia), and various cardiac arrhythmias. Diarrhea may be noted, as may abdominal discomfort or pain, headache, malaise, and drowsiness were common symptoms, neuralgic pain may be the earliest most severe, it may occur with confusion, disorientation, aphasia and mental clouding.

Toxicity can often be managed by discontinuing digitalis, determining serum potassium levels, and, if indicated, replenishing potassium. The main toxins in Digitalis are the two chemically similar cardiac glycosides: digitoxin and digoxin. Like other cardiac glycosides, these toxins exert their effects by inhibiting the ATPase activity of a complex of transmembrane proteins that form the sodium-potassium ATPase pump, (Na^+/K^+-ATPase). Inhibition of the Na^+/K^+-ATPase, in turn, causes a rise not only in intracellular Na^+ but also in calcium, which in turn results in increased force of myocardial muscle contractions. In other words, at precisely the right dosage, Digitalis toxin can cause the heart to beat more strongly. However, digitoxin, digoxin and several other cardiac glycosides, such as ouabain, are known to have steep dose-response curves, *i.e*., minute increases in the dosage of these drugs can make the difference between an ineffective dose and a fatal one.

Symptoms of *Digitalis* poisoning include a low pulse rate, nausea, vomiting, and uncoordinated contractions of different parts of the heart, leading to cardiac arrest and finally death [25, 36].

CONCLUSION: The current review discussed the chemical constituents and pharmacological effects of *Digitalis purpurea* as important medicinal plants with a wide range of medicinal uses. Cardiac glycosides or cardenolides are natural products contained in *Digitalis purpurea*, although leaves from *Digitalis species* are the most important source of these compounds. Due to their effectiveness in the treatment of heart insufficiency, cardenolides from *Digitalis purpurea* are still used very extensively worldwide.

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CONFLICT OF INTEREST: Nil

REFERENCES:

1. Orhan IE: Biotechnological production of secondary plant metabolites. Bentham ebook 2012: 107.
2. Al-Snafi AE: Medicinal plants possessed antiinflammatory antipyretic and analgesic activities (part 2)-plant based review. Sch Acad J Pharm 2016; 5(5): 142-158.
3. Snafi, IAJPS%202017,%20(01),%2067-73.pdf.
4. Bagrov AY and Fedorova OV: Cardenolide and bufadienolide ligands of the sodium pump. How they work together in NaCl sensitive hypertension. Front Biosci 2005; 10: 2250-2256.
5. Lacassie E, Marquet P, Martin-Dupont S, Gaulier JM and Lachatre G: A non-fatal case of intoxication with foxglove, documented using Liquid Chromatography-Electrospray-Mass-Spectrometry. J Forensic Sci 2000; 45: 1154-1158.
6. Buckalew VM: Endogenous digitalis-like factors. An Histori 2005.
7. The plant list, a working list of all plant species, Digitalis *purpurea*, http://www.theplantlist.org/tpl/record/kew-2768087.
8. ITIS report, *Digitalis lanata*, http: //www. itis. gov/servlet /SingleRpt/ SingleRpt? search _topic=TSN&search_value =33583.
9. Al-Snafi AE: Nutritional and therapeutic importance of *D. carota*- A review. IOSR J of Pharmacy 2017; 7(2): 72-88.
10. Al-Snafi AE: Chemical constituents and pharmacological effects of *Dalbergia sissoo* - A review. IOSR Journal of Pharmacy 2017; 7(2): 59.
11. ITIS report, *Digitalis purpurea*, http://www.itis.gov/servlet/SingleRpt/SingleRpt?search_topic=TSN&search_value=33585
12. Khare CP: Indian medicinal plants: An illustrated dictionary. Springer Publication 2007: 214.
13. U. S. National Plant Germplasm System, *Digitalis purpurea*, https://npgsweb.arsgrin.gov/gringlobal/taxonomy detail.aspx?13986
14. http://www.yourarticlelibrary.com/biology/glycoside/digitalis-sources-cultivation-and-uses-with-diagram/49758.
15. http://www.yourarticlelibrary.com/biology/glycoside/digitalis-sources-cultivation-and-uses-with-diagram/49758.
16. Franco AJ: Nova Flora de Portugal, Sociedade Astória, Lisboa, Vol. II, 1984: 245-247.
17. U.S.National Plant Germplasm System, *Digitalis lanata*, https://npgsweb.arsgrin.gov/gringlobal/taxonomydetail.aspx?13979
18. Kırmızıbekmez H, Celep E, Masullo M, Bassarello C, ilada EY and Piacente S: Phenylethyl glycosides from *Digitalis lanata*. Helvetica Chimica Acta 2009; 92: 1845-1852.
19. Lee JY, Woo E and Kang KW: Screening of new chemopreventive compounds from *Digitalis purpurea*. Pharmazie 2006; 61(4): 356-358.
20. Kokate CK: Practical Pharmacognosy. Delhi, Vallabh Prakashan, 1996: 107-111.
21. Cardiac Glycoside Plant Poisoning: Medscape reference. Retrieved 3 July 2012.
22. Bagrov AY and Fedorova OV: Cardenolide and bufadienolide ligands of the sodium pump. How they work together in NaCl sensitive hypertension. Front Biosci 2005; 10: 2250-2256.
23. Hood WB, Dans A, Guyatt GH, Jaeschke R and McMurray JJ: Digitalis for treatment of congestive heart

failure in patients in sinus rhythm. Cochrane Database Syst Rev 2004; (2):CD002901.
24. https://www.webmd.com/vitamins-supplements/ingredientmono-287-foxglove.aspx?activeingredientid=287&activeingredientname=foxglove.
25. Negi SJ, Bisht VK, Bhandari AK and Sundriyal RC: Determination of mineral contents of *Digitalis purpurea* L. and *Digitalis lanata* Ehrh. Journal of Soil Science and Plant Nutrition 2012; 12: 469.
26. Whalen K, Finkel R and Panavelil TA: Lippincott illustrated reviews: Pharmacology, Wolters Kluwer, Edition 6th, 2015: 263-265.
27. Smith TW: The fundamental mechanism of inotropic action of *Digitalis*. Therapie 1989; 44: 431-435.
28. Jorgensen PL, Hakansson KO and Karlish SJ: Structure and mechanism of Na, K-ATPase: functional sites and their interactions. Annu Rev Physiol 2003; 65: 817-849.
29. Lindholm P, Gullbo J and Claeson P: Selective cytotoxicity evaluation in anticancer drug screening of fractionated plant extracts. J Biomol Scr 2002; 7: 333-340.
30. Hauptman PJ and Kelly RA: Cardiovascular drugs, *Digitalis*. Circulation 1999; 99: 1265-1270.
31. Johansson S, Lindholm P, Gullbo J, Larsson R, Bohlin L and Claeson P: Cytotoxicity of digitoxin and related cardiac glycosides in human tumor cells. Anticancer Drugs 2001; 12(5): 475-483.
32. Srivastava M, Eidelman O, Zhang J, Paweletz C, Caohuy H, Yang Q, Jacobson KA, Heldman E, Huang W, Jozwik C, Pollard BS and Pollard HB: Digitoxin mimics gene therapy with CFTR and suppresses hypersecretion of IL-8 from cystic fibrosis lung epithelial cells. Proc Natl Acad Sci USA 2004; 101(20): 7693-7698.
33. Wang JK, Portbury S, Thomas MB, Barney S, Ricca DJ, Morris DL, Warner DS and Lo DC: Cardiac glycosides provide neuroprotection against ischemic stroke: discovery by a brain slice-based compound screening platform. Proc Natl Acad Sci USA 2006; 103(27): 10461-10466.
34. Pierre SV, Yang C, Yuan Z, Seminerio J, Mouas C, Garlid KD, Dos-Santos P and Xie Z: Ouabain triggers preconditioning through activation of the Na^+, K^+ -ATPase signaling cascade in rat hearts. Cardiovasc Res 2007; 73(3): 488-496.
35. Ebaid GM, Faine LA, Diniz YS, Rodrigues HG, Galhardi CM, Ribas BO, Fernandes AA and Novelli EL: Effects of digitonin on hyperglycemia and dyslipidemia induced by high-sucrose intake. Food Chem Toxicol 2006; 44(2): 293-299.
36. Mason DT and Braunwald E: Studies on *Digitalis*, X: effects of ouabain on forearm vascular resistance and venous tone in normal subjects and in patients in heart failure. J Clin Invest 1964; 43: 532-43.

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