

Review on Digitalis in Contemporary Medicine : Benefits, Risks, and Decline Clinical use

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<https://doi.org/10.55041/ijst.v2i3.418>

Cite this Article: Biswas, G. (2026). Review on Digitalis in Contemporary Medicine : Benefits, Risks, and Decline Clinical use. International Journal of Science, Strategic Management and Technology, 02(03). <https://doi.org/10.55041/ijst.v2i3.418>

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Abstract

Digitalis purpurea (commonly known as foxglove) is a well-known medicinal plant that has played a crucial role in cardiovascular pharmacology. It is the primary natural source of cardiac glycosides such as digoxin and digitoxin, widely used in the management of heart failure and arrhythmias. This article provides an overview of its phytochemistry, pharmacological actions, therapeutic applications, and toxicity in modern medicine.

Keywords- Digitalis, pharmacological, digoxin, heart diseases.

Introduction

This article is about the flowering plant *Digitalis purpurea*. It is a biennial herb belonging to the family Plantaginaceae. Historically, it gained prominence in the 18th century when William Withering, an English physician, systematically studied its effects and introduced it for the treatment of heart-related conditions. Since then, *Digitalis* has become a classical example of a plant-derived drug in modern medicine. when its cardiotonic properties were identified. Today, its derivatives remain important in clinical practice, especially for managing cardiac disorders. The common name of digitalis is foxglove. It is the first source of heart medicine digoxin. A category of medicines extracted from fairy glove plants are called digitalin. Bohemians use foxglove to treat eczema (1). Foxglove has various medicinal uses but it is also very toxic to humans and other mammals such that consumption can cause serious illness or death (2).

The plant is a rich source of cardiac glycosides, particularly digoxin and digitoxin, which exert powerful effects on the heart. These compounds are widely used for managing conditions such as congestive heart failure and atrial fibrillation by improving cardiac contractility and regulating heart rhythm. Despite its therapeutic importance, *Digitalis* is also known for its narrow therapeutic index, meaning the difference between a safe dose and a toxic dose is very small. Therefore, its use requires careful dosage monitoring and clinical supervision.

Digitalis acts by inhibiting the Na^+/K^+ -ATPase enzyme in pharmacological terms. It leads to an increase in intracellular calcium in cardiac cells. This results in a positive inotropic effect (increased force of contraction) and a negative chronotropic effect (reduced heart rate).

Digitalis is primarily used in the management of congestive heart failure and atrial fibrillation. However, due to its narrow therapeutic index, it requires careful dose monitoring to avoid toxicity. In short: Digitalis is a plant-derived cardiotonic drug that improves heart function but must be used cautiously. The other name of digitalis are as follows:

Purple foxglove

Lady's glove

Fairy gloves

Witch's gloves

Foxgloves

Historical Background and Source:

In modern pharmacology digitalis originated from the foxglove plant, particularly *Digitalis purpurea* and *Digitalis lanata*. the main clinically used of digitalis glycoside is digoxin Contemporary pharmacology more on standardized pharmaceutical digoxin formulations with defined pharmacokinetics, dosage, monitoring, and safety parameters and focuses less on crude plant preparations (3). 20th Century overcoming the toxicity risks of using the raw plant because of active digitalis glycosides are purified and refined for precise dosing, overcoming the toxicity risks of using the raw plant.



Fig no 1.0 Digitalis

Classification of Digitalis in Modern Pharmacology

Digitalis refers to a group of cardiac glycosides obtained mainly from plants like *Digitalis purpurea* and *Digitalis lanata*. It is primarily used in heart failure and arrhythmias.

1. Based on Source (Origin)

A. Natural Digitalis Glycosides

Digoxin

Digitoxin

B. Semi-synthetic Derivatives

Acetyldigoxin

Methyldigoxin

2. Based on Duration of Action

A. Short-acting

Ouabain

B. Intermediate-acting

Digoxin

C. Long-acting

Digitoxin

3. Based on Pharmacokinetics (Half-life & Lipid Solubility)

A. High Lipid Solubility

Digitoxin

Long half-life, hepatic metabolism

B. Moderate Lipid Solubility

Digoxin

Moderate duration, renal excretion

C. Low Lipid Solubility

Ouabain

Poor oral absorption, rapid action

4. Based on Clinical Use

A. Used in Heart Failure

Digoxin

B. Used in Arrhythmias (Atrial fibrillation/flutter)

Digoxin

Organoleptic Properties of Digitalis (Crude Drug – Leaves)

For pharmacognosy identification there are Organoleptic (sensory) properties are evaluated using sight, smell, taste, and touch.



Fig No 1.1 crude drug leaves

1. Colour

Upper surface: Dark green

Lower surface: Pale green / greyish

Dried leaves: Olive green to brownish green

2. Odour

Slight / faint odour

Sometimes described as tea-like

3. Taste

Bitter (due to cardiac glycosides like Digoxin)

Slightly acrid

4. Size & Shape

Shape: Ovate or lanceolate

Length: 10–35 cm

Margin: Crenate or serrate

Apex: Acute

Base: Decurrent

5. Surface Characteristics

Upper surface: Rough and wrinkled

Lower surface: Hairy (pubescent) with prominent veins

6. Texture

Thin but tough

Slightly leathery

7. Fracture

Short and brittle when dried

Organoleptic Properties of Digitalis (According to Modern Pharmacology)

In modern pharmacology, Digitalis is considered mainly in its purified drug forms (like Digoxin), so organoleptic properties are described for active pharmaceutical ingredients (APIs) rather than crude leaves.



Fig NO 1.2 Appearance of Digitalis Preparations (e.g., Digoxin)

1. Colour

White to off-white crystalline powder (pure drug)

Tablets: White or slightly coloured (depending on formulation)

2. Odour

Odourless

3. Taste

Bitter taste (characteristic of cardiac glycosides)

4. Physical Nature

Crystalline solid

Stable under normal conditions but sensitive to light and moisture

5. Solubility

Slightly soluble in **water**

More soluble in **alcohol and organic solvents**

6. Dosage Forms (Modern Use)

Tablets (e.g., Digoxin)

Injection (IV preparation)

Oral solution (rare)

Mechanism of action digitalis:

1.Primary Molecular Target- Na^+/K^+ -ATPase pump located on the cardiac myocyte membrane and it is the main target of digitalis (especially Digoxin).

Pumps 3 Na^+ out and 2 K^+ in

Maintains low intracellular Na^+

Helps regulate ionic balance and electrical activity

2. Step-by-Step Cellular Mechanism:

Step 1: Inhibition of Na^+/K^+ -ATPase

Digitalis binds to the extracellular side of the pump

Pump activity decrease.

Na^+ accumulates inside the cell

Step 2: Effect on $\text{Na}^+/\text{Ca}^{2+}$ Exchanger (NCX)

Normally: NCX removes Ca^{2+} by exchanging it with Na^+

Now: High intracellular Na^+ reduces NCX efficiency

Less Ca^{2+} is removed from the cell

Step 3: Increase in Intracellular Calcium

Ca^{2+} accumulates in cytoplasm

More Ca^{2+} stored in **sarcoplasmic reticulum (SR)**

During next heartbeat → massive Ca^{2+} release

Strong myocardial contraction

Step 4: Positive Inotropic Effect

↑ **Force of contraction (Positive inotropy)**

↑ **Stroke volume**

↑ **Cardiac output**

5.Neurohormonal Effects

Digitalis also:

↓ Sympathetic activity

↓ Renin release

Improves **neurohormonal balance** in heart failure

Hemodynamic Effects

In Heart Failure:

↑ Cardiac output

↓ End-diastolic volume

↓ Venous pressure

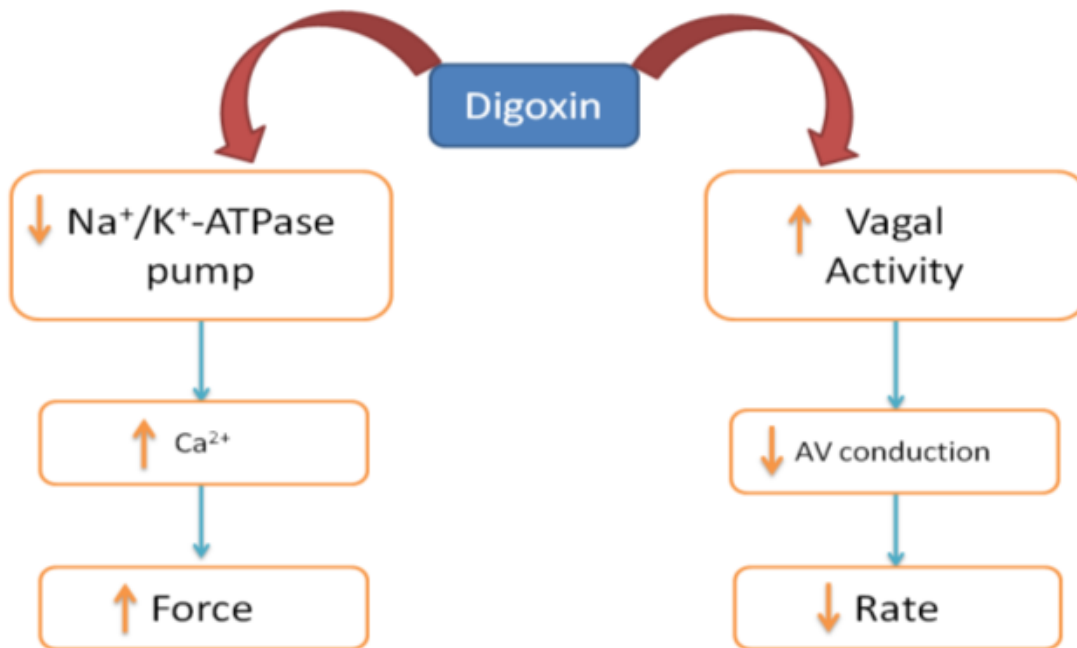


Fig No 1.3

Pharmacological activities:

1. Heart contraction-Digitalis directly effects on contractility of myocardial, so it decrease.

It increase force of contraction.

Heart rate is decreased by digitalis.

Bradycardia is more marked in chf patients.

2. Blood vessels -Digoxin has mild direct vasoconstriction action.

It increase blood pressure

Therapeutic Uses in Contemporary Pharmacology:

Heart Failure- Digoxin is mainly used in the treatment of heart failure. where digitalis had a much broader. This reflects a major change from older practice.

Arrhythmias – Digitalis is also used in the treatment of arrhythmia.

Atrial Fibrillation

ventricular rate control, In atrial fibrillation, by digoxin still has value for particularly in selected cannot tolerate more aggressive blood-pressure-lowering drugs. patients such as those with concomitant heart failure. It is not favoured generally when rapid rate is control, because intravenous diltiazem acts fastly that condition(4)

Clinical Advantages

It improves cardiac contractility, helps control ventricular rate in atrial fibrillation, still offers several clinically meaningful advantages. and m helpful in patients with heart failure who have low blood pressure, where beta blockers or non-dihydropyridine calcium channel blockers may be harder to use or up-titrate. (5)

Limitations and Safety Concern:

Toxicity can present with nausea, vomiting, anorexia, fatigue, visual disturbances, and a wide range of arrhythmias. Risk rises in older adults and in patients with renal impairment, hypokalemia, hypercalcemia, or hypomagnesemia. Because toxicity may occur even at lower levels in susceptible patients, interpretation must always include symptoms, ECG findings, renal function, and electrolyte status.(3)

Drug Interactions and Monitoring

A major theme in modern pharmacology is not simply what digoxin does, but how carefully it must be monitored. Drug interactions, renal impairment, and electrolyte abnormalities can all alter exposure and toxicity risk. Monitoring typically includes renal function, serum electrolytes, pulse rate, ECG when indicated, and serum digoxin concentration in patients with suspected toxicity, dose changes, or unstable clinical status. The FDA label explicitly advises periodic assessment of renal function and electrolytes and recommends serum-level checking when toxicity is suspected. (3)

Why Digitalis Use Has Declined

The decline in digitalis use does not mean the drug has become ineffective; rather, the therapeutic environment has changed. Modern cardiovascular care now includes medications that improve survival and disease progression more robustly in heart failure, while atrial fibrillation management has broader options for rate control and rhythm management. Consequently, digoxin has become a supportive or adjunctive drug, reserved for specific clinical scenarios rather than routine universal use. (3)

Future Directions

Recent reviews suggest that cardiac glycosides continue to attract interest beyond traditional cardiology, including exploratory work in oncology and precision medicine. That said, these areas remain investigational, and the established, guideline-supported role of digitalis today remains primarily cardiovascular. Its future in modern pharmacology will likely depend on better patient selection, concentration-guided therapy, and pharmacogenomic or precision-use approaches rather than a return to widespread empirical prescribing.(6)

13. Future Perspectives

Research is ongoing to explore:

Safer dosing strategies

Personalized medicine approaches

Potential roles beyond cardiology

Conclusion

Digitalis continues to be a valuable drug in modern pharmacology, although its role has become more limited and specialized. Its effectiveness in improving cardiac contractility and controlling heart rate ensures its continued use in selected patients. Careful monitoring and dose adjustment are essential to maximize benefits and minimize toxicity.



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