

IDENTIFICATION AND EXTRACTION PROCESS OF CARDIAC GLYCOSIDES FROM FOXGLOVE PLANTS

Susi Febrianti¹, Fathi Farhan², Juarfianti³, Sabrina Audry

Salfa⁴, Rema Elviona⁵, Ika Meruya Kusuma⁶

1,2,3,4,5,6 Undergraduate Pharmacy Study Program, National Institute of Science and Technology, South Jakarta
juarfianti.arfah@gmail.com

Received: May 22, 2024; Accepted: June 10, 2024; Published: Jul 12, 2024;

Abstract: Foxglove (*Digitalis* spp.) is a plant known for its cardiac glycoside content, which has been used in medicine for centuries. Cardiac glycosides, such as digoxin and digitoxin, are the main components that have a therapeutic effect on the cardiovascular system. This research examines the cardiac glycoside content of various *Digitalis* species, with a focus on extraction methods, isolation and characteristics of these compounds. Methods used include high-performance liquid chromatography (HPLC), mass spectrometry (MS), and nuclear magnetic resonance (NMR). The analysis results showed that *Digitalis purpurea* and *Digitalis lanata* were the main sources of cardiac glycosides. Digoxin and digitoxin were isolated and identified as the main active components. Pharmacological studies show that this compound interacts with the sodium-potassium ATPase pump, which increases cardiac contractility and is used in the treatment of heart failure and arrhythmias. Cardiac glycosides from the foxglove plant play an important role in cardiovascular therapy. Further research is needed to develop more efficient extraction methods and understand the deeper mechanisms of action, as well as potential side effects associated with long-term use.

Keywords: foxglove, cardiac glycosides, extraction



This is an open-access article under the [CC-BY 4.0](#) licenses

Introduction

Heart glycosides are a group of bioactive compounds known for their effects on the cardiovascular system, especially in the treatment of heart failure and arrhythmia. This compound works by increasing the strength of heart contractions and regulating heart rhythms, so it is essential in clinical therapy for patients with certain cardiovascular conditions [1]. Heart glycosides, such as digoxin and digitoxin, are steroid derivatives that are capable of increasing myocardial contraction efficiency without causing significantly increased oxygen requirements [2]. This makes them an important component in the treatment of heart disease.

The foxglove plant (*Digitalis purpurea*) is a major source of heart glycoside that has long been used in traditional and modern medicine. The history of its use can be traced back to the 18th century when William Withering first documented the therapeutic effects of foxglove leaves in the treatment of edema and heart failure [3]. Modern research has confirmed the therapeutic potential of cardiac glycosides, and products such as digoxin have become the gold standard in treating congestive cardiac failure and some types of arrhythmia [4]. However, despite this, there is a difference in effectiveness and safety between traditional and modern clinical uses.

The correct identification of the heart glycoside in plant extracts is essential to ensure the purity and effectiveness of the final product. Modern techniques such as high-performance liquid chromatography (HPLC) and mass spectrometry have facilitated this identification process with a high degree of accuracy [5]. Recent studies show that the HPLC method is capable of separating and identifying heart glycosides with excellent precision, allowing researchers to evaluate phytochemical profiles of foxglove plant extracts comprehensively [6]. It is important to ensure that only the desired compounds are consumed by the patient, reducing the risk of unwanted side effects.

The process of extraction of heart glycosides from the foxglove plant involves several important steps that must be optimized to ensure maximum results. Extraction usually begins with the drying and grinding of foxglove leaves, followed by the extraction process using organic solvents such as methanol or ethanol [7]. After extraction, purification techniques such as liquid-liquid fractionation and crystallization are used to isolate high-purity glycosides [8]. Literature studies show that the extraction and insulation methods used significantly affect the yield and purity of the final product, so research continues to develop more efficient and environmentally friendly techniques.

The study of literature is important in this research as it provides a strong theoretical foundation and up-to-date information about the techniques that have been used and tested in previous research. Through the study of literature, researchers can identify the most effective and innovative methods, avoid the same mistakes, and build on existing knowledge to develop better processes in cardiac glycoside isolation [9]. The study of literature also helps in understanding how variations in environmental conditions, solvent types, and purification techniques can affect the quality and quantity of glycosides produced, providing valuable insights for researchers in optimizing extraction and insulation processes.

Methods

This study employs a literature review methodology to gather and analyze data regarding glikosida jantung from foxglove (*Digitalis purpurea*) plants. Literature studies enable researchers to examine various long-term studies that support the identification, elaboration, and isolation of glikosida jantung, thereby providing rigorous theoretical frameworks and new information. Through the analysis of many creditable academic sources such as journals, books, and academic publications, this study can identify the most innovative and effective techniques for the extraction and glikosida jantung process. In addition to that, this approach helps to overcome shared challenges and develop existing knowledge to develop more environmentally friendly and efficient methods. The comprehensive review of the literature in this area enables researchers to achieve more optimal and applicable results in the fields of pharmacy and pharmacology by utilizing critical insights from earlier research.

Results and discussion

Based on a literature study, the steps for identifying and extracting cardiac glycosides from foxglove (*Digitalis purpurea*) were obtained.

Identification Of Cardiac Glycosides

Identification of cardiac glycosides involves several stages from extraction to chemical analysis:

UV-Vis Spectroscopy:

This technique is used to detect the presence of glycosides based on the specific wavelengths absorbed by the compound. Glycosidesheart usually shows characteristic absorption peaks in the UV-Vis range.

IR Spectroscopy

Infrared (IR) spectroscopy provides information about functional groups in cardiac glycoside molecules, such as hydroxyl and carbonyl groups.

NMR Spectroscopy

This technique is used to determine molecular mass and provide information about the structure of glycoside compound fragments.

Structure And Function Of Cardiac Glycosides

Cardiac glycosides consist of two main components: aglycone (or genin) and glycone. Aglycones are usually steroids, while glycones are sugars. This structure allows cardiac glycosides to interact with

the Na+/K+-ATPase enzyme in cardiac cell membranes, leading to an increase in intracellular calcium and strengthening cardiac contractions.

Cardiac Glycoside Extraction Process

Extraction of cardiac glycosides from natural materials, such as plant leaves or flowers, involves several major steps including material collection, sample preparation, extraction, and purification. Following are the details of these steps:

1. Collection of Plant Material

Material plant Whichcontaining cardiac glycosides, such as *Digitalis purpurea* or *Nerium oleander* leaves, should be collected at the right time, usually when the glycoside content reaches its peak.

2. Sample Preparation

a. Drying

Fresh plant material is dried in a shady, well-ventilated area to prevent degradation of the active compounds. This drying can be done naturally or by using an oven at a low temperature (40-50°C).

b. Milling

Once dry, the plant material is ground into a fine powder to increase surface area and extraction efficiency.

3. Extraction

a. Extraction Solvent

Organic solvents such as ethanol, methanol, or a mixture of water and ethanol are used to extract cardiac glycosides from plant powders. The choice of solvent depends on the solubility of the cardiac glycoside in the solvent.

b. Extraction Process

Extraction can be done by several methods:

Maceration

The plant powder is soaked in the solvent at room temperature for several days with periodic stirring.

Soxhletation

The plant powder is extracted continuously with a hot solvent using a soxhlet device for several hours.

Ultrasonication

Use ultrasonic waves to speed up the extraction process by breaking down plant cells and releasing cardiac glycosides into the solvent.

Filtration

Once the extraction process is complete, the mixture is filtered to separate the liquid extract from the plant dregs.

4. Purification

a. Solvent Evaporation

Liquid extract obtained from filtration Then evaporated using a rotary evaporator to remove the solvent and obtain a concentrated extract.

b. Fractionation

The concentrated extract is then further separated using chromatography techniques, such as:

Column Chromatography

The extract is flowed through a column containing a stationary phase (silica gel or resin) and separated based on differences in polarity.

High Performance Liquid Chromatography (HPLC)

Uses high pressure to separate extract components with high resolution and faster speed.

5. Identification and Characterization

The cardiac glycoside components in the purified extract were identified using spectroscopic techniques such as UV-Vis, IR, NMR, and MS to determine the structure and purity of the compound.

6. Biological Activity Test Biochemical Test

The biological activity of extracts containing cardiac glycosides was tested to ensure effectiveness and safety. This test can include testing the activity of the Na^+/K^+ -ATPase enzyme or in vitro and in vivo tests in animal models.

7. Extraction Process

The process of extracting cardiac glycosides from foxglove involves several stages:

a. Collection and Drying

Foxglove leaves are collected and dried to reduce the content of water which can affect extraction efficiency.

b. Destruction

The dried leaves are crushed into a fine powder to increase the contact surface with the solvent.

c. Solvent extraction

Extraction carried out using organic solvents such as ethanol, methanol, or chloroform.

The powdered leaves are soaked in solvent and stirred at room temperature or heated to increase extraction efficiency.

d. Filtration and Evaporation

The mixture is extracted and then filtered to separate the solution from the solid material.

The solvent is then evaporated to obtain a crude extract.

e. Purification

Crude extracts are purified using chromatography, such as column chromatography or high-performance liquid chromatography (HPLC), to separate cardiac glycosides from other compounds.

Analysis Methods

Some analytical methods suitable for use in the identification and purification of cardiac glycosides from foxglove include:

1. High Performance Liquid Chromatography (HPLC)

HPLC is a highly efficient purification method that can separate glycosides based on polarity and molecular size.

2. Thin Layer Chromatography (TLC)

TLC is used to monitor progress of purification and identify compounds based on the distance traveled on the chromatography plate.

3. Bioassays

Testing the biological activity of cardiac glycosides in animal or cell models to confirm their pharmacological effectiveness.

Identification and extraction of cardiac glycosides from foxglove plants is a complex but important process to produce compounds with high pharmacological activity. The use of analytical techniques such as spectroscopy and chromatography ensures that the isolated compounds have the purity and efficacy required for medical use.

Overall, various techniques have been used to extract and purify cardiac glycosides from *Digitalis purpurea*, including conventional methods such as maceration and soxhletation as well as modern methods such as ultrasonication and supercritical fluid extraction. The main benefit of cardiac glycosides is in the treatment of heart failure and arrhythmias, but research also shows other

therapeutic potential. Extraction method application is very important. Choosing the right one to get optimal and pure results.

The following is a review of 10 journals about cardiac glycosides in foxglove plants, their benefits, and how to isolate glycosides:

1. Digitalis Glycosides : Mechanisms of Action and Clinical Use

Source: Journal of Cardiovascular Pharmacology.

Summary: This journal discusses the mechanism of action of cardiac glycosides from Digitalis purpurea and their use in clinical medicine. The main benefits include strengthening heart contractions and stabilizing heart rhythm in patients with congestive heart failure.

Isolation: Extraction using ethanol followed by fractionation using column chromatography.

2. Cardiac Glycosides from Digitalis purpurea : Isolation and Structural Characterization

Source: Phytochemistry

Summary : This study describes methods for the isolation and structural characterization of cardiac glycosides from Digitalis purpurea. The main benefit is its potential in heart failure therapy.

Isolation: Using soxhletation with methanol followed by HPLC for purification.

3. Therapeutic Use of Digitalis Glycosides in Modern Medicine

Source: International Journal of Medical Sciences.

Summary : This article highlights the use of cardiac glycosides from Digitalis in modern medicine, especially in regulating heart function and reducing symptoms of heart failure.

Isolation: Maceration in ethanol then fractionation by thin layer chromatography (TLC).

4. Advanced Methods for the Isolation of Cardiac Glycosides from Digitalis

Source: Journal of Natural Products

Summary : This journal introduces the latest techniques for the isolation of cardiac glycosides from Digitalis, including ultrasonication methods to increase extraction efficiency.

Isolation: Ultrasonication with methanol-water mixture followed by purification using HPLC.

5. Pharmacokinetics and Pharmacodynamics of Digitalis Glycosides

Source: Clinical Pharmacology & Therapeutics

Summary : This article evaluates the pharmacokinetics and pharmacodynamics of the cardiac glycosides of Digitalis, demonstrating the importance of appropriate dosing to avoid toxicity.

Isolation: Use of a rotary evaporator for solvent evaporation after extraction with ethanol.

6. Comparative Study of Different Extraction Methods for Cardiac Glycosides from Digitalis Purpurea

Source: Journal of Pharmacognosy and Phytotherapy

Summary : This study compared various methods of extracting cardiac glycosides from Digitalis, finding that soxhletation with ethanol provided the best results.

Isolation: Soxhletation with ethanol and fractionation using column chromatography.

7. Cardiac Glycosides: Benefits Beyond Heart Disease

Source: Bioorganic & Medicinal Chemistry

Summary : This article explores the additional cardiac glycoside benefits of Digitalis, including anticancer and anti-viral potential.

Isolation: Extraction with ethanol followed by purification using liquid chromatography.

8. Extraction and Purification of Digitalis Glycosides Using Supercritical Fluid Extraction

Source: Journal of Supercritical Fluids

Summary : This journal reviews the use of supercritical fluid extraction for the isolation of cardiac glycosides from Digitalis, offering a more environmentally friendly and efficient method.

Isolation: Supercritical CO₂ extraction followed by purification with HPLC.

9. Clinical Efficacy of Digitalis Glycosides in Heart Failure Management

Source: American Heart Journal

Summary : This article discusses the clinical effectiveness of Digitalis cardiac glycosides in the management of heart failure, emphasizing the importance of therapeutic monitoring.

Isolation: Maceration with ethanol, then purification using high performance liquid chromatography (HPLC).

10. Recent Advances in the Extraction and Purification of Cardiac Glycosides from Digitalis

Source: Phytochemical Analysis

Summary : This journal reviews recent advances in extraction and purification techniques for cardiac glycosides from Digitalis, including the use of modern extraction technologies such as microwave-assisted extraction.

Isolation: Extraction with the help of microwaves followed by purification with HPLC.

Conclusion

This study emphasizes the significance of techniques used to identify and extract cardiac glycosides from the foxglove plant (*Digitalis purpurea*). The identification of cardiac glycosides entails use spectroscopic techniques, such as UV-Vis, IR, and NMR, to detect and evaluate the chemical composition of these molecules. Cardiac glycosides are composed of an aglycone (genin) and a glycone, enabling them to interact with the Na⁺/K⁺-ATPase enzyme in the membranes of cardiac cells. This interaction leads to an augmentation of heart contractions. The extraction procedure comprises multiple phases, which encompass the gathering and desiccation of botanical matter, pulverization into a refined powder, and extraction utilizing organic solvents such as ethanol or methanol. Following the extraction process, the extract solution is separated from the solid material using filtration and evaporation. Subsequently, the extract undergoes purification using chromatography methods such as High-Performance Liquid Chromatography (HPLC) and Thin-Layer Chromatography (TLC). Contemporary techniques like ultrasonication and supercritical fluid extraction have been employed to enhance the efficiency of extraction. Bioactivity assays verify the pharmacological efficacy of the extracted glycosides. This research utilizes a range of spectroscopic and chromatographic techniques to confirm that the extracted glycoside molecules have the necessary purity and effectiveness for medical purposes.

References

- [1]. Brunton, L.L., Chabner, B., & Knollmann, B.C. (2011). *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill.
- [2]. Devlin, T. M. (2010). *Textbook of Biochemistry with Clinical Correlations*. Wiley.
- [3]. Gul, M., et al. (2021). "Comparative Analysis of Cardiac Glycosides in Digitalis Species." *Journal of Chromatography A*, 1638, 461773.
- [4]. Harborne, J. B. (1998). *Phytochemical Methods: A Guide to Modern Techniques of Plant Analysis* (3rd ed.). London: Chapman and Hall.
- [5]. Katzung, B. G. (2012). *Basic and Clinical Pharmacology*. McGraw Hill.
- [6]. King, A.M., & Aaron, C.K. (2015).
- [7]. Toxicity and Management of Cardiac Glycosides. *Toxicon*, 97, 2-12.
- [8]. Krenn, L., & Kopp, B. (2021). "Glycoside Extraction Methods and Bioactivity." *Phytochemistry Reviews*, 20(3), 875-888.
- [9]. Li, J., & Wang, H. (2022). "Genetic Engineering of Digitalis for Enhanced Glycoside Production." *Plant Biotechnology Journal*, 20(4), 748-759.
- [10]. Martínez, J.P., et al. (2022). "Sustainable Cultivation Techniques for Foxglove Plants." *Agricultural Sciences*, 13(3), 124-134.
- [11]. Mroczeck, T. (2015). Recent Advances in the Detection, Identification, and Quantification of Cardiovascular Drugs. *BioMed Research International*, 2015, Article ID 218765.
- [12]. Murray, R.K., Granner, D.K., Mayes, P.
- [13]. A., & Rodwell, V. W. (2012). *Harper's Illustrated Biochemistry*. McGraw-Hill.
- [14]. Pandey, R., & Chaturvedi, A. (2016). Isolation and Identification of Cardiac Glycosides from

Medicinal Plants. International Journal of Pharmacognosy and Phytochemical Research, 8(7), 1112-1116.

- [16]. Patel, P., et al. (2022). "Advanced Analytical Techniques for Cardiac Glycoside Profiling." Analytical Chemistry, 94(5), 2354-2362.
- [18]. Prassas, I., & Diamandis, E. P. (2008). Novel Therapeutic Applications of Cardiac Glycosides. Nature Reviews Drug Discovery, 7(11), 926-935.
- [19]. Rang, H. P., Dale, M. M., Ritter, J. M., Flower, R. J., & Henderson, G. (2012). Rang and Dale's Pharmacology (7th ed.). Edinburgh: Churchill Livingstone.
- [20]. Robbers, JE, Speedie, MK, & Tyler,
- [21]. VE (1996). Pharmacognosy and Pharmacobiotechnology. Williams & Wilkins.
- [22]. Segall, A., & Balague, C. (2004). High Performance Liquid Chromatography (HPLC) for Cardiac Glycoside Analysis. Journal of Chromatography A, 1028(1), 1-20.
- [23]. Sharma, V., et al. (2021). "Isolation and Characterization of Bioactive Glycosides from Digitalis lanata." Journal of Natural Products, 84(2), 556- 565.
- [24]. Smith, T. W., & Antman, E. M. (1997). Digitalis (Cardiac Glycosides) in the Management of Cardiovascular Disorders. Circulation, 96(3), 127-132.
- [25]. Steinkamp, J. A., & Wagner, H. (2005). Cardiac Glycosides and Their Mode of Action. In H. Wagner & G. UlrichMerzenich (Eds.), Evidence and Rational Based Research on Chinese Drugs (pp. 285-300). Berlin: Springer.
- [26]. Wang, Z., et al. (2020). "Foxglove plants produce heart medicine. Can science do it better?" University at Buffalo.