THE EFFECT OF *DRACEANA ARBOREAL* HYDROALCOHOLIC EXTRACT ON SPONTANEOUSLY BEATING RAT ATRIA AND PERFUSED RABBIT HEART PREPARATION.

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A PROJECT SUBMITTED TO THE DEPARTMENT OF PHARMACOLOGY AND TOXICOLOGY IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR AWARD OF DOCTOR OF PHARMACY (PHARMD) DEGREE DEPARTMENT OF PHARMACOLOGY AND TOXICOLOGY, FACULTY OF PHARMACY, UNIVERSITY OF BENIN, BENIN CITY, NIGERIA.

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CERTIFICATION

We certify that this project work titled "*the effect of Dracaena arborea on a spontaneously beating rat atria and perfused rabbit heart preparation*" was carried out by Osariemen Endurance in the Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Benin, Benin City, Nigeria.

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ANTI-PLAGIARISM CERTIFICATION

We the undersigned attest and declare that the thesis of Osariemen Endurance titled "the effect of *Dracaena arborea* on a spontaneously beating rat atria and perfused rabbit heart**"** has successfully passed the anti-plagiarism test and does not violate any copyright regulations.

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DEDICATION

I dedicate this work to God Almighty, my Baal Perazim, to the Osariemen family and to the house of MFMCF UNIBEN.

ACKNOWLEDGEMENT

I express my deepest gratitude to God Almighty for His grace, strength, and faithfulness in bringing me to this stage of my life and enabling me to achieve a dream that once seemed so far away.

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ABSTRACT

Dracaena arborea is traditionally used in African medicine for treating cardiovascular ailments, including palpitations and irregular heartbeat, yet its antiarrhythmic mechanism remains poorly defined. Cardiac arrhythmias, a major cause of morbidity and mortality, often result from disturbances in ion channel activity, altered cardiac excitability, or impaired conduction. Although conventional antiarrhythmic drugs effectively target these pathways, their side effects and limited accessibility have prompted growing interest in plant-based alternatives. This study investigated the *in vitro* antiarrhythmic potential of the methanol stem bark extract of *Dracaena arborea* using isolated animal heart preparations.

Isolated rat atrial tissues were mounted in an organ bath containing aerated Locke-Ringer's solution at 37°C, while contractile responses were recorded using a force transducer connected to a data acquisition system. The effect of cumulative concentrations of the extract on cardiac contractility and rhythm was assessed. Additionally, the Langendorff-perfused rabbit heart model was employed to evaluate the extract's influence on experimentally induced arrhythmias. Data were expressed as mean ± SEM and analysed using GraphPad Prism, with statistical significance set at $P < 0.05$.

The results demonstrated that the *Dracaena arborea* extract produced a concentration-dependent reduction in the force and rate of contraction of isolated rat atria. In the Langendorff model, the extract significantly suppressed arrhythmic activity induced by adrenaline and calcium overload, showing a stabilizing effect on cardiac rhythm comparable to standard antiarrhythmic agents such as propranolol. These findings suggest that the extract may exert its action through modulation of calcium influx or β-adrenergic receptor blockade.

Understanding the molecular mechanisms underlying its antiarrhythmic properties could contribute to the development of novel plant-based therapeutic agents for arrhythmia and vascular dysfunction.

CHAPTER ONE

INTRODUCTION AND LITERATURE REVIEW

1.1 INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide, accounting for nearly one-third of global deaths annually (WHO, 2021). These disorders encompass a wide spectrum of pathological conditions of the heart and blood vessels, including hypertension, coronary artery disease, heart failure, and cardiac arrhythmias. In low- and middle-income countries such as Nigeria, the burden of CVDs has been rising steadily due to urbanization, changes in lifestyle, and limited access to preventive healthcare (Ogah et al., 2015). Beyond their medical consequences, CVDs impose a heavy socioeconomic burden by reducing productivity, increasing healthcare expenditure, and straining fragile health systems.

Among the various manifestations of CVDs, cardiac arrhythmias occupy a position of critical concern. Cardiac arrhythmia refers to any abnormality in the initiation or conduction of electrical impulses within the heart, leading to disturbances in rhythm, rate, or conduction sequence. These disturbances may present as tachyarrhythmias (excessively rapid heart rhythms), bradyarrhythmias (abnormally slow rhythms), atrial or ventricular fibrillation, or conduction blocks. While some arrhythmias are relatively benign, others are life-threatening, predisposing patients to sudden cardiac death, stroke, or progressive heart failure (Zipes and Jalife, 2014). The risk of arrhythmias increases with age, structural heart disease, electrolyte imbalances, and drug toxicity. Importantly, in developing nations, late diagnosis and inadequate treatment often worsen outcomes.

The physiological basis of arrhythmias lies in the complex interplay of cardiac ion channels and the conduction system. The coordinated depolarization and repolarization of

cardiomyocytes are tightly regulated by sodium, potassium, and calcium fluxes across the cell membrane. Disturbances in these ionic currents—whether due to ischemia, fibrosis, genetic mutations, or pharmacological agents—can lead to triggered activity, re-entry phenomena, or conduction blocks, which underlie the majority of arrhythmic conditions (Katz, 2010). Understanding these mechanisms has guided the development of antiarrhythmic drugs and experimental models that simulate cardiac rhythm disorders.

Pharmacological treatment of arrhythmias is largely guided by the Vaughan–Williams classification system, which categorizes drugs into four major classes: sodium channel blockers (Class I), beta-adrenergic blockers (Class II), potassium channel blockers (Class III), and calcium channel blockers (Class IV). Although these drugs are clinically effective, their use is often limited by significant drawbacks such as narrow therapeutic indices, organ toxicity, proarrhythmic effects, and multiple drug interactions (Nattel, 2017). For instance, quinidine and other Class I drugs may themselves precipitate arrhythmias, while amiodarone is associated with pulmonary, hepatic, and thyroid toxicities. These challenges highlight the urgent need for safer and more effective therapeutic options.

In Nigeria and other parts of sub-Saharan Africa, access to modern antiarrhythmic therapy is further constrained by high costs and limited availability of cardiology specialists. Consequently, many populations continue to rely on medicinal plants for managing cardiovascular disorders, a practice rooted in indigenous knowledge systems. Indeed, several pharmacological agents currently in use originated from plant sources, including digoxin from Digitalis purpurea and reserpine from Rauwolfia serpentina. This underscores the potential of medicinal plants as reservoirs of bioactive molecules that may yield new antiarrhythmic agents.

Dracaena arborea, a perennial plant belonging to the family Asparagaceae, is widely distributed in West and Central Africa. It has long been utilized in traditional medicine for the

management of diverse conditions including hypertension, sexual dysfunction, and inflammatory disorders (Beppe et al., 2019). Phytochemical analyses have identified flavonoids, saponins, glycosides, and terpenoids in this plant—classes of compounds with known cardiovascular activity. For example, flavonoids have been reported to modulate ion channel function and reduce oxidative stress, while saponins may stabilize cell membranes and influence cardiac excitability. These properties suggest a possible role of D. *arborea* in the modulation of cardiac rhythm, although scientific validation remains limited.

Experimental pharmacology provides a critical platform for investigating the potential antiarrhythmic properties of medicinal plants. In vitro models such as isolated rat atrial preparations in organ baths and perfused rabbit hearts using the Langendorff apparatus have been widely employed to study cardiac function and arrhythmogenesis. These models offer controlled environments that allow precise measurement of heart rate, contractility, conduction, and rhythm in response to pharmacological interventions (Curtis and Walker, 2018). By applying these methods, it is possible to assess the direct actions of plant extracts on cardiac tissues, thereby generating reliable data on their potential therapeutic utility.

Given the growing prevalence of cardiovascular diseases and the limitations of current antiarrhythmic therapies, research into plant-derived alternatives is timely and necessary. Investigating the antiarrhythmic effect of *Dracaena arborea* on isolated rat atria and perfused rabbit heart models will provide valuable insight into its pharmacological profile and support the scientific basis for its traditional use in cardiovascular disorders. Ultimately, such studies could contribute to the discovery of novel agents with safer and more affordable therapeutic options for populations at risk of arrhythmias.

1.2 Definition of Arrhythmia and Cardiac Conduction

1.2.1 Definition of arrhythmia

The term arrhythmia refers to any disturbance in the normal rhythm of the heart, whether in the rate, regularity, site of impulse origin, or sequence of cardiac activation. Under physiological conditions, the heartbeat is generated and propagated by specialized cells of the cardiac conduction system, ensuring synchronized contraction of the atria and ventricles. In arrhythmic states, this orderly sequence is disrupted, leading to abnormalities in impulse formation or conduction. Clinically, arrhythmias may manifest as palpitations, dizziness, syncope, chest pain, or, in severe cases, sudden cardiac death (Katz, 2010).

Arrhythmias are broadly classified according to their mechanism, site of origin, or effect on heart rate. They may arise from enhanced automaticity, triggered activity, or re-entrant circuits within the myocardium (Zipes and Jalife, 2014). Depending on the site of origin, arrhythmias can be atrial, junctional, or ventricular. Based on rate, they are commonly divided into bradycardia (heart rate below 60 beats per minute) and tachycardia (rate above 100 beats per minute). While some arrhythmias, such as isolated premature atrial contractions, are benign, others, such as ventricular fibrillation, are life-threatening emergencies requiring immediate intervention.

The importance of arrhythmias in clinical medicine cannot be overstated. They contribute significantly to morbidity and mortality, often complicating underlying heart diseases such as ischemic heart disease, hypertensive cardiomyopathy, or valvular disorders. In Nigeria and other resource-limited settings, late diagnosis and limited access to specialized care further exacerbate outcomes in patients with arrhythmias. Understanding what constitutes normal

cardiac rhythm and conduction is therefore crucial in appreciating the pathophysiology of arrhythmias.

1.2.2 Overview of the normal cardiac conduction system

The heart possesses an intrinsic conduction system that ensures rhythmic and coordinated contractions of the atria and ventricles. This conduction system is composed of specialized myocardial cells that possess automaticity, excitability, and conductivity. The primary components include the sinoatrial (SA) node, atrioventricular (AV) node, bundle of His, right and left bundle branches, and the Purkinje fiber network.

1. **Sinoatrial node (sa node):**

   Located in the right atrium near the opening of the superior vena cava, the SA node is regarded as the natural pacemaker of the heart. It generates spontaneous action potentials due to its inherent automaticity, driven by the gradual depolarization of pacemaker cells via inward sodium and calcium currents. Under normal conditions, the SA node sets the rhythm of the heart at approximately 60–100 beats per minute in adults (Guyton and Hall, 2020).

2. **Atrial conduction pathways:**

   From the SA node, impulses spread through atrial muscle fibers and specialized internodal tracts, ensuring depolarization of both atria. This synchronous contraction of the atria contributes to ventricular filling, a process sometimes referred to as the "atrial kick."

Atrioventricular node (av node):

Located at the lower part of the interatrial septum near the coronary sinus, the AV node serves as the only electrical connection between the atria and ventricles under normal physiological conditions. The conduction through the AV node is deliberately slow, introducing a brief delay that allows for complete atrial contraction and ventricular filling before the onset of ventricular systole. This delay is critical for maintaining cardiac efficiency.

3. **Bundle of his and bundle branches:**

   From the AV node, impulses are transmitted into the bundle of His, which traverses the fibrous skeleton of the heart and enters the interventricular septum. The bundle then bifurcates into right and left bundle branches. These branches conduct impulses rapidly towards the apex of the heart and into the ventricular myocardium.

4. **Purkinje fibers:**

   The bundle branches terminate in Purkinje fibers, which distribute the electrical impulse throughout the ventricular myocardium. Purkinje fibers are characterized by rapid conduction velocities, ensuring that both ventricles contract almost simultaneously. This coordinated contraction is essential for efficient ejection of blood into the pulmonary artery and aorta.

The sequence of activation—beginning with the SA node, proceeding through the atria, AV node, bundle of His, bundle branches, and Purkinje fibers—produces the characteristic electrical pattern recorded as the electrocardiogram (ECG). The P wave corresponds to atrial depolarization, the QRS complex represents ventricular depolarization, and the T wave reflects ventricular repolarization. Any disturbance in this sequence can give rise to arrhythmias.

The cardiac conduction system is modulated by autonomic inputs. Sympathetic stimulation increases heart rate and conduction velocity through beta-adrenergic receptors, while parasympathetic (vagal) input decreases heart rate and slows AV nodal conduction via muscarinic receptors. Electrolyte concentrations, especially of potassium, calcium, and sodium, also play key roles in determining conduction properties. Abnormalities in autonomic regulation or electrolyte balance may predispose to arrhythmogenesis.

In summary, the normal conduction system of the heart provides the framework for regular, coordinated cardiac activity. Arrhythmias arise when there is disruption of impulse generation at the pacemaker sites, abnormal propagation through the conduction pathways, or altered recovery of excitability in myocardial cells. A clear understanding of the physiology of conduction is therefore fundamental for appreciating how pharmacological interventions—including antiarrhythmic drugs and plant-derived agents—may restore or maintain rhythm.

1.3 Cardiac Arrhythmias

1.3.1 Types of cardiac arrhythmias

Cardiac arrhythmias represent a broad spectrum of rhythm disorders arising from abnormalities in impulse formation, conduction, or both. They are commonly categorized according to rate, site of origin, and mechanism of disturbance.

1. **Bradyarrhythmias**

   These refer to heart rhythms with a rate slower than 60 beats per minute in adults. They are often due to sinus node dysfunction (sinus bradycardia, sinus arrest, or sinoatrial block) or impaired conduction through the atrioventricular node (first, second, or third-degree heart block). Severe bradyarrhythmias may cause dizziness, syncope, or even cardiac arrest due to reduced cardiac output (Mangrum and DiMarco, 2000).

2. **Tachyarrhythmias**

Tachyarrhythmias occur when the heart beats faster than 100 beats per minute. They may originate from the atria, atrioventricular junction, or ventricles. Examples include atrial fibrillation, atrial flutter, paroxysmal supraventricular tachycardia, and ventricular tachycardia. Ventricular fibrillation is a particularly life-threatening form that results in chaotic electrical activity and loss of effective cardiac pumping, requiring immediate defibrillation (Zipes and Jalife, 2014).

3. **Premature Beats**

These are early depolarizations originating outside the SA node. Premature atrial contractions (PACs) and premature ventricular contractions (PVCs) are common and may be asymptomatic or symptomatic depending on frequency and underlying cardiac health.

4. **Conduction Abnormalities**

Arrhythmias may also result from abnormal conduction pathways. Re-entrant tachycardias, such as Wolff–Parkinson–White syndrome, occur due to accessory conduction pathways that allow impulses to bypass normal nodal delays. Bundle branch blocks are another example of conduction disturbances that alter the normal activation sequence of the ventricles.

5. **Fibrillatory Arrhythmias**

Atrial fibrillation and ventricular fibrillation are characterized by uncoordinated, rapid, and irregular electrical activity. While atrial fibrillation predisposes to thromboembolic complications, ventricular fibrillation is immediately fatal unless reversed.

1.3.2 Pathophysiology of cardiac arrhythmias

The development of arrhythmias can be explained by disturbances in impulse formation or conduction, often involving one or more of the following mechanisms:

Enhanced automaticity.

Normally, the SA node generates impulses at a regular rate. However, increased automaticity may occur when other myocardial cells acquire pacemaker activity, often due to ischemia, electrolyte disturbances, or sympathetic overactivity. These ectopic foci can outpace the SA node, leading to tachyarrhythmias.

1. **Triggered activity**

   Abnormal afterdepolarizations during or after repolarization may precipitate premature action potentials. Early afterdepolarizations (EADs) occur during phase 2 or 3 of the action potential, while delayed afterdepolarizations (DADs) occur during phase 4. Both mechanisms can cause repetitive firing and sustained arrhythmias, as seen with digitalis toxicity or prolonged QT syndromes (January and Riddle, 1989).

2. **Re-Entry phenomena**

   Re-entry is one of the most important mechanisms in clinical arrhythmias. It occurs when an impulse continues to circulate in a loop within myocardial tissue due to heterogeneities in conduction velocity or refractory periods. Re-entry can sustain

tachyarrhythmias such as atrial flutter, atrioventricular nodal re-entrant tachycardia, and ventricular tachycardia.

3. **Conduction blocks**

Partial or complete block in impulse transmission through the atrioventricular node or His–Purkinje system may result in bradyarrhythmias or dropped beats. Third-degree AV block, for example, results in dissociation between atrial and ventricular rhythms.

On a molecular level, arrhythmias are closely linked to dysfunction of ion channels controlling sodium, potassium, and calcium currents. Genetic mutations in channel proteins (channelopathies) are increasingly recognized in inherited arrhythmia syndromes such as long QT syndrome, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia (Antzelevitch et al., 2005).

1.3.3 Diagnosis of cardiac arrhythmias

The diagnosis of arrhythmias requires careful correlation of symptoms with objective measures of cardiac rhythm. The **electrocardiogram (ECG)** remains the cornerstone diagnostic tool, allowing real-time evaluation of rhythm, rate, conduction intervals, and wave morphology. Ambulatory monitoring with Holter recorders or event recorders is useful in patients with intermittent arrhythmias.

Electrophysiological studies provide detailed mapping of conduction pathways and arrhythmogenic foci, especially in patients being considered for catheter ablation therapy. Echocardiography, cardiac MRI, and laboratory testing (electrolytes, thyroid function) may also provide supporting evidence of underlying structural or metabolic contributors.

Clinically, arrhythmias are often suspected based on symptoms such as palpitations, syncope, lightheadedness, chest discomfort, or unexplained fatigue. In emergency settings, hemodynamic instability and ECG evidence of malignant arrhythmias necessitate immediate intervention.

In conclusion, cardiac arrhythmias represent diverse disturbances in rhythm that range from benign to fatal. Their mechanisms include abnormalities of automaticity, triggered activity, re-entry, and conduction block. Accurate diagnosis and characterization of arrhythmias are essential for effective treatment. Understanding their pathophysiology also provides the basis for developing new pharmacological agents, including those derived from medicinal plants such as *Dracaena arborea*.

1.4 Classification of Antiarrhythmic Drugs

Antiarrhythmic drugs are pharmacological agents used to prevent, suppress, or correct disturbances in cardiac rhythm. Their use is guided by the underlying mechanism of arrhythmias, which may involve abnormal impulse generation or conduction. The most widely accepted system for categorizing these drugs is the Vaughan–Williams classification, which divides antiarrhythmics into four major classes based on their primary electrophysiological effects on cardiac tissue (Vaughan-Williams, 1984).

1.4.1 Vaughan-williams classification

Class I: Sodium channel blockers

Class I agents act by inhibiting fast sodium channels in myocardial cells, thereby slowing phase 0 depolarization and reducing conduction velocity. They are subdivided into three groups based on their effects on the action potential duration:

- **Class Ia** (e.g., quinidine, procainamide, disopyramide): These drugs moderately depress phase 0 depolarization and prolong the action potential and refractory period. They are effective against both atrial and ventricular arrhythmias but carry a risk of proarrhythmia, particularly torsades de pointes.

- **Class Ib** (e.g., lidocaine, mexiletine): These agents shorten the action potential duration and have a greater effect on ischemic or depolarized ventricular tissue. They are primarily used for ventricular arrhythmias, especially following myocardial infarction.

- **Class Ic** (e.g., flecainide, propafenone): These drugs markedly slow conduction without significant effect on repolarization. They are potent suppressors of supraventricular and ventricular arrhythmias but may increase mortality in patients with structural heart disease.

Class I drugs are widely used in clinical practice but are often limited by their narrow therapeutic window, risk of exacerbating arrhythmias, and systemic adverse effects such as hypotension, dizziness, or gastrointestinal disturbances (Nattel, 2017).

Class II: Beta-adrenergic blockers

Class II antiarrhythmics function by antagonizing beta-adrenergic receptors in the heart. This reduces sympathetic stimulation, slows sinoatrial (SA) nodal firing, and prolongs atrioventricular (AV) nodal conduction. Commonly used beta-blockers include propranolol, metoprolol, and atenolol.

These drugs are particularly effective in arrhythmias associated with increased sympathetic activity, such as sinus tachycardia, paroxysmal supraventricular tachycardia, and certain post-myocardial infarction ventricular arrhythmias. Additionally, beta-blockers improve survival in

patients with heart failure and reduce sudden cardiac death. However, they may cause bradycardia, hypotension, fatigue, and bronchospasm in susceptible individuals.

Class III: Potassium channel blockers

Class III agents prolong the repolarization phase (phase 3) of the cardiac action potential by blocking potassium efflux, thereby extending the refractory period. Examples include amiodarone, sotalol, and dofetilide.

Amiodarone is notable for its efficacy against a broad spectrum of arrhythmias, including atrial fibrillation, ventricular tachycardia, and refractory cases. Its pharmacological effects are complex, as it also exhibits properties of Class I, II, and IV agents. Despite its effectiveness, amiodarone use is associated with significant toxicity, including pulmonary fibrosis, hepatotoxicity, thyroid dysfunction, and skin reactions, which limits long-term administration (Nattel, 2017).

Sotalol combines beta-blocking activity with potassium channel inhibition, providing dual antiarrhythmic effects. Dofetilide selectively prolongs repolarization and is mainly used for rhythm control in atrial fibrillation under strict monitoring due to the risk of QT prolongation and torsades de pointes.

Class IV: Calcium channel blockers

Class IV agents selectively inhibit L-type calcium channels, predominantly affecting nodal tissue. This results in slowing of AV nodal conduction and prolongation of the refractory period. Verapamil and diltiazem are commonly used Class IV drugs.

These agents are effective in treating supraventricular tachycardias, including atrial fibrillation with rapid ventricular response and paroxysmal supraventricular tachycardia. They are

generally well-tolerated but may cause hypotension, bradycardia, and, rarely, atrioventricular block in predisposed individuals.

Table 4: Overview of Antiarrhythmic Drugs: Mechanisms, Uses, and Limitations

Class	**Mechanism of Action**	**Subclasses / Examples**	**Primary Uses**	**Key Adverse Effects / Limitations**
Class I Sodium Channel Blockers	Block fast Na^+ channels → slow Phase 0 depolarization → ↓ conduction velocity	**Ia:** Quinidine, Procainamide, Disopyramide **Ib:** Lidocaine, Mexiletine **Ic:** Flecainide, Propafenone	**Ia:** Atrial + Ventricular arrhythmias **Ib:** Ventricular arrhythmias (esp. post-MI) **Ic:** Supraventricular + Ventricular arrhythmias	Narrow therapeutic window, Proarrhythmia (e.g., torsades de pointes), Hypotension, Dizziness, GI upset
Class II Beta-Adrenergic Blockers	Block β-receptors → ↓ sympathetic activity → ↓ SA firing & ↓ AV conduction	Propranolol, Metoprolol, Atenolol	Sinus tachycardia, PSVT, Post-MI arrhythmias	Bradycardia, Hypotension, Fatigue, Bronchospasm
Class III Potassium Channel Blockers	Block K^+ efflux → Prolong Phase 3 repolarization → ↑ Refractory period	Amiodarone, Sotalol, Dofetilide	Atrial fibrillation, Ventricular tachycardia	Amiodarone toxicity (lung, liver, thyroid), QT prolongation, Torsades de pointes
Class IV Calcium Channel Blockers	Block L-type Ca^{2+} channels → Slow AV conduction → ↑ Refractory period	Verapamil, Diltiazem	Supraventricular tachycardias (e.g., AF with RVR, PSVT)	Hypotension, Bradycardia, Possible AV block

1.4.2 Limitations of conventional antiarrhythmic therapy

Despite the proven efficacy of antiarrhythmic drugs, their use is constrained by several challenges. First, many agents carry a risk of proarrhythmia, paradoxically precipitating the very arrhythmias they are intended to suppress. Second, drug toxicity affecting the liver, lungs, thyroid, or other organs limits long-term therapy. Third, cost and availability can be prohibitive in resource-limited settings, particularly in sub-Saharan Africa. Additionally, inter-individual variability in drug response may necessitate frequent monitoring, dose adjustments, and ECG follow-up.

These limitations have prompted ongoing research into alternative strategies, including the investigation of plant-derived compounds with potential antiarrhythmic properties. Several medicinal plants contain flavonoids, saponins, and alkaloids that modulate cardiac ion channels, stabilize membranes, or exert antioxidant effects, which could provide safer and more accessible options for rhythm management.

In summary, the Vaughan–Williams classification provides a clear framework for understanding the pharmacological actions of conventional antiarrhythmic drugs. While these agents are effective, their limitations underscore the need for alternative therapies. Research into plant-based antiarrhythmic agents, such as *Dracaena arborea*, offers a promising avenue for the development of safer, affordable, and effective cardiac rhythm modulators.

1.5 Experimental Models Used in Assessing Antiarrhythmic Activity

1.5.1 In vivo models

In vivo models refer to the use of living organisms, usually small mammals such as rats, mice, guinea pigs, or rabbits, to study cardiac rhythm and pharmacological interventions in a systemic environment. These models allow the assessment of drug effects on the entire cardiovascular

system, including neurohumoral regulation, autonomic tone, and hemodynamic changes. Common in vivo methods for evaluating antiarrhythmic activity include drug-induced arrhythmias using agents such as aconitine, ouabain, or calcium chloride, and ischemia-reperfusion models that simulate myocardial infarction-induced arrhythmias.

While in vivo models provide valuable information on systemic pharmacokinetics, drug metabolism, and potential toxicity, they have limitations in isolating specific cardiac electrophysiological effects. Factors such as neurohumoral influence, anesthesia, and variability in heart rate can confound results. Therefore, in vivo studies are generally used in combination with in vitro experiments to provide a more complete understanding of antiarrhythmic potential (Curtis and Walker, 2018).

1.5.2 In vitro models

In vitro models are experimental setups in which cardiac tissues or whole hearts are isolated from the organism and studied under controlled laboratory conditions. These models allow precise measurement of cardiac electrical activity, contractility, and response to pharmacological agents without the confounding influence of systemic factors. In vitro approaches are considered more reproducible, cost-effective, and ethically manageable compared to in vivo studies.

The primary in vitro models used for assessing antiarrhythmic activity include **isolated atrial tissue in organ baths** and the **perfused heart using Langendorff apparatus**. These models provide direct insight into the electrophysiological effects of drugs or plant extracts, including changes in heart rate, contractile force, conduction velocity, and the incidence of induced arrhythmias.

1.5.2.1 Isolated atrial tissue in organ bath

The isolated atrial preparation is one of the most widely used in vitro models for studying cardiac rhythm and drug effects. In this technique, atrial tissue—usually the left atrium of a rat—is excised and mounted in an organ bath containing a physiologically buffered solution, such as Locke-Ringer's Lactate, maintained at controlled temperature(30 degrees celsius) and aeration(with pure oxygen gas). The tissue is connected to a force transducer, allowing continuous recording of contractile activity via a physiograph or digital acquisition system.

This model is particularly suitable for investigating the effects of drugs or plant extracts on **automaticity**, **contractility**, and **arrhythmogenesis**. By applying graded doses of a test substance, researchers can observe concentration changes in atrial contractions, conduction intervals, and spontaneous rhythmicity. Comparisons are often made with a standard antiarrhythmic agent, such as quinidine or propranolol, to validate the observed effects. The organ bath setup also allows pharmacological manipulation, such as altering ion concentrations or adding adrenergic agonists/antagonists, to elucidate mechanisms of action (Katz, 2010).

Advantages of this model include simplicity, reproducibility, and the ability to perform multiple interventions on a single tissue sample. However, limitations exist: the model represents only atrial tissue, lacks ventricular components, and does not account for systemic metabolism or autonomic regulation. Despite these constraints, the isolated atrial tissue model remains a cornerstone in the preclinical evaluation of antiarrhythmic agents.

1.5.2.2 Perfused heart (langendorff preparation)

The Langendorff-perfused heart is a sophisticated in vitro model that allows the study of the whole isolated heart under controlled perfusion conditions. In this setup, the heart—commonly from a rabbit, guinea pig, or rat—is excised and retrogradely perfused via the aorta with

oxygenated physiological solution. Perfusion can be either constant pressure or constant flow, ensuring adequate coronary perfusion and maintenance of spontaneous heart activity.

This preparation enables the direct assessment of cardiac rhythm, conduction, and contractile function without the influence of systemic variables. Researchers can induce arrhythmias pharmacologically (e.g., with aconitine, ouabain, or calcium chloride) and evaluate the protective or suppressive effects of test substances. Electrodes and force transducers can record ECG tracings and contractile responses, providing quantitative data on heart rate, conduction intervals, refractory periods, and arrhythmia incidence (Curtis and Walker, 2018).

The Langendorff model offers several advantages over simpler tissue preparations. It provides a complete cardiac context, including atrial and ventricular interactions, AV nodal conduction, and realistic myocardial architecture. It is particularly useful for studying **ventricular arrhythmias**, conduction blocks, and pharmacological modulation of the entire cardiac cycle. Limitations include the technical complexity, requirement for rapid heart excision to prevent ischemic damage, and absence of neurohumoral influences.

1.5.2.3 Other related models

Other in vitro models exist for specialized studies of cardiac rhythm, including:

- Papillary muscle preparations: used to assess contractility and repolarization.
- Monolayer cardiac cell cultures: useful for electrophysiological studies at the cellular level.
- Patch-clamp techniques: allow high-resolution analysis of ion channel function in isolated cardiomyocytes.

While these models provide valuable mechanistic insight, they are generally considered complementary to the organ bath and Langendorff preparations when evaluating antiarrhythmic activity.

In vitro models, particularly the isolated atrial organ bath and Langendorff-perfused heart, provide robust, reproducible platforms for assessing the antiarrhythmic potential of pharmacological agents, including plant extracts such as *Dracaena arborea*. These models enable precise measurement of cardiac responses under controlled conditions, minimizing systemic confounding factors while allowing detailed evaluation of mechanisms, dose-dependence, and comparison with standard drugs. Together with in vivo studies, they form the foundation of experimental pharmacology in cardiovascular research.

1.6 The Heart and Its Physiology

1.6.1 Anatomy of the heart

The heart is a hollow, muscular organ located in the mediastinum, responsible for pumping blood throughout the body. It is divided into four chambers: the right atrium, right ventricle, left atrium, and left ventricle. The atria serve as receiving chambers, collecting deoxygenated blood from the systemic circulation via the superior and inferior vena cava into the right atrium, and oxygenated blood from the pulmonary veins into the left atrium. The ventricles act as pumping chambers, propelling blood into the pulmonary artery and aorta, respectively.

Blood flow within the heart is regulated by valves that prevent backflow. The atrioventricular valves—tricuspid on the right and mitral on the left—permit unidirectional blood flow from atria to ventricles. The semilunar valves—pulmonary and aortic—control blood ejection from the ventricles into the great arteries. Proper valve function ensures efficient circulation and contributes to maintaining normal cardiac rhythm.

Embedded within the cardiac musculature is the conduction system, responsible for initiating and propagating electrical impulses. Key components include the sinoatrial (SA) node, the atrioventricular (AV) node, the bundle of His, the right and left bundle branches, and the Purkinje fibers. The SA node, located in the right atrium near the superior vena cava, acts as the natural pacemaker. Impulses from the SA node spread through the atria to the AV node, which introduces a delay to ensure complete atrial contraction before ventricular excitation. The impulse then travels via the bundle of His, branches, and Purkinje fibers to activate the ventricles synchronously. Disruptions in any part of this conduction system can lead to arrhythmias (Katz, 2010).

1.6.2 Electrophysiology of the heart

The electrophysiological properties of the heart are dictated by the **action potentials** of cardiac cells, which differ between nodal and working myocardial cells.

1. **Nodal cells (SA and AV nodes):**

   Nodal cells possess automaticity, allowing them to generate spontaneous action potentials without external stimuli. The depolarization of nodal cells is primarily mediated by **slow calcium currents (L-type Ca^{2+} channels)**, while repolarization involves **potassium efflux**. Sodium plays a minor role in depolarization in these cells. The rhythmic firing of the SA node sets the pace for the heart, while the AV node modulates conduction velocity, providing the essential atrioventricular delay.

2. **Working myocardial cells (atrial and ventricular myocytes):**

Action potentials in working cells are characterized by distinct phases:

- **Phase 0 (rapid depolarization):** Initiated by rapid influx of sodium through fast sodium channels, leading to a steep upstroke.

- **Phase 1 (initial repolarization):** Brief partial repolarization due to transient outward potassium currents.
- **Phase 2 (plateau phase):** Balance between inward calcium currents and outward potassium currents; critical for contraction.
- **Phase 3 (repolarization):** Predominantly potassium efflux restores resting membrane potential.
- **Phase 4 (resting potential):** Stable negative membrane potential maintained by potassium conductance, with minimal sodium and calcium leakage.

This coordinated electrical activity ensures timely atrial and ventricular contractions, producing efficient blood ejection. Any abnormalities in ion channel function, phase durations, or conduction pathways can result in arrhythmias.

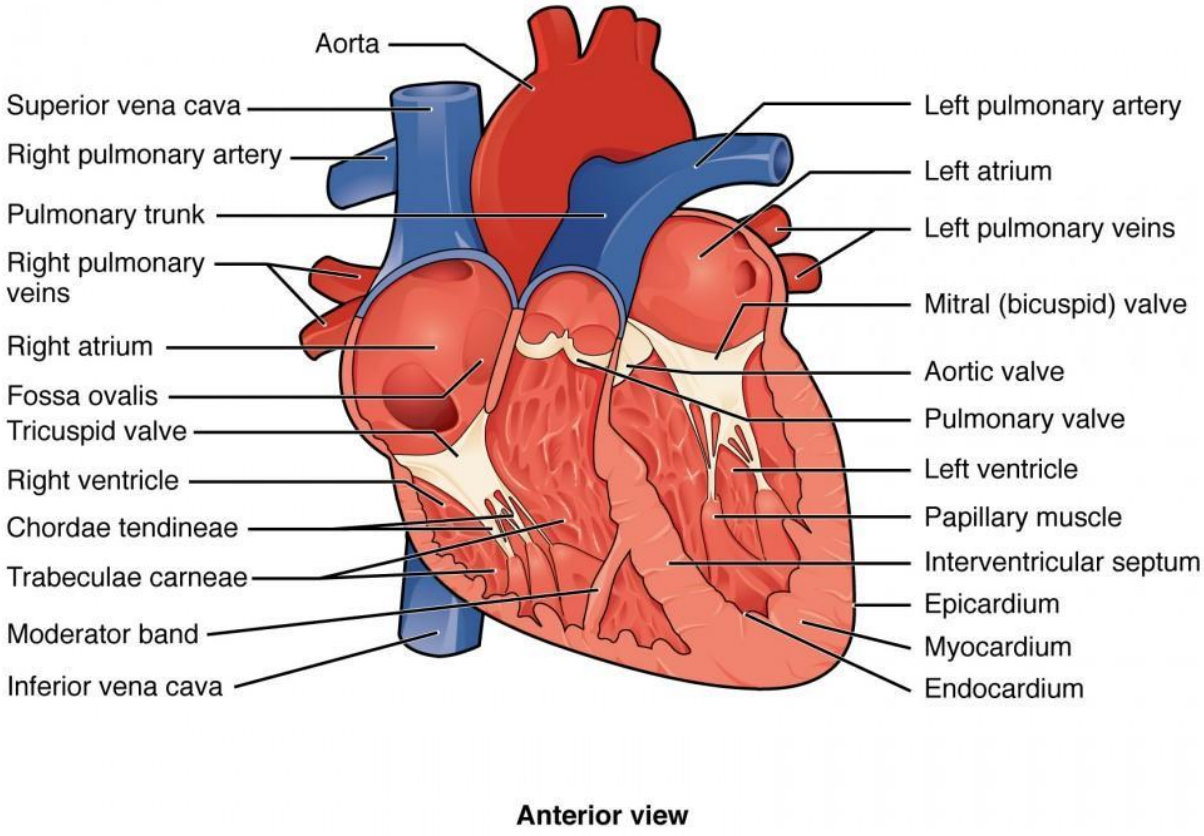

Figure 1: Illustrative diagram of the human heart showing anatomical structures (Source: Lumen Learning, n.d.).

The visual representation enhances comprehension of the conduction system and helps relate anatomical and electrophysiological principles to arrhythmogenesis.

The heart's anatomy and electrophysiology form the foundation for understanding normal rhythm and the pathogenesis of arrhythmias. The coordination between nodal pacemaker activity and myocardial contraction ensures effective blood circulation. Disruptions in this system, whether due to structural, ionic, or pharmacological factors, can result in rhythm disturbances. Understanding these fundamentals is essential for interpreting experimental data from in vitro models such as isolated atrial preparations and Langendorff-perfused hearts, which are used to evaluate potential antiarrhythmic agents, including plant extracts like *Dracaena arborea*.

1.7 Medicinal Plants in Cardiovascular Pharmacology

Medicinal plants have played a pivotal role in the development of pharmacotherapy for cardiovascular diseases (CVDs). Historically, indigenous systems of medicine in Africa, Asia, and Europe have utilized plants to manage hypertension, heart failure, arrhythmias, and other cardiac conditions. In modern pharmacology, plant-derived compounds have served as sources for many clinically important drugs, such as digoxin from Digitalis purpurea for heart failure and reserpine from Rauwolfia serpentina for hypertension. The interest in phytochemicals stems from their diverse biological activities, structural diversity, and potential for reduced toxicity compared to synthetic drugs (Ekor, 2014).

1.7.1 General role of phytochemicals in cardiovascular therapy

Phytochemicals are biologically active compounds found in plants, including flavonoids, alkaloids, saponins, terpenoids, glycosides, and phenolic acids. These compounds exert cardiovascular effects through multiple mechanisms:

1. **Modulation of ion channels**

   Flavonoids and alkaloids can influence sodium, potassium, and calcium channels, affecting cardiac excitability, conduction velocity, and action potential duration. This modulation can prevent abnormal depolarizations and stabilize cardiac rhythm, suggesting potential antiarrhythmic effects.

2. **Vasodilation and blood pressure regulation**

   Certain phytochemicals enhance endothelial nitric oxide production, inhibit angiotensin-converting enzyme (ACE), or block calcium influx in vascular smooth muscle. These actions contribute to vasodilation, reduced afterload, and improved cardiac output, indirectly benefiting arrhythmia management.

3. **Antioxidant and anti-inflammatory effects**

   Oxidative stress and inflammation are key contributors to arrhythmogenesis and cardiac remodeling. Polyphenols, saponins, and flavonoids scavenge free radicals, inhibit lipid peroxidation, and reduce pro-inflammatory cytokine levels, thereby protecting myocardial tissue and preserving conduction system integrity.

4. **Anti-apoptotic and cardioprotective effects**

Some phytochemicals modulate signalling pathways involved in cell survival, such as Bcl-2 and caspase pathways, reducing cardiomyocyte apoptosis during ischemic or oxidative stress conditions. This contributes to long-term maintenance of cardiac structure and rhythm.

Overall, these diverse mechanisms highlight the potential of medicinal plants as sources of antiarrhythmic and cardioprotective agents. They offer advantages such as multi-targeted effects, accessibility, and affordability, particularly in regions with limited healthcare resources.

1.7.2 Examples of plant-derived antiarrhythmic or cardioprotective agents

1. ***Digitalis purpurea*** **(Foxglove)**

Digitalis glycosides, particularly digoxin, increase myocardial contractility by inhibiting the Na^+/K^+-ATPase pump (Gheorghiade et al., 2004). This leads to increased intracellular calcium and improved cardiac output. Additionally, digoxin enhances vagal tone, slows AV nodal conduction, and helps control ventricular rate in atrial fibrillation, making it a classic plant-derived antiarrhythmic.

2. ***Rauwolfia serpentina***

The alkaloid reserpine lowers blood pressure by depleting catecholamines in sympathetic nerve endings (Menon et al., 2022). While primarily an antihypertensive agent, its modulation of autonomic tone can indirectly reduce arrhythmogenic stimuli associated with sympathetic overactivity.

3. **Crataegus species (Hawthorn)**

Hawthorn extracts contain flavonoids and oligomeric procyanidins that enhance coronary blood flow, improve myocardial contractility, and exhibit antioxidant properties (Holubarsch et al., 2008). Preclinical studies indicate potential in preventing ischemia-induced arrhythmias and improving cardiac function.

4. ***Allium sativum*** **(Garlic)**

Garlic's organosulfur compounds exert vasodilatory, anti-inflammatory, and antioxidant effects, which contribute to cardioprotection (Ried and Fakler, 2014). Some studies have reported modulation of cardiac conduction and reduction of arrhythmogenic events in animal models.

5. ***Camellia sinensis*** **(Green Tea)**

Catechins from green tea act as antioxidants, reduce oxidative stress, and improve endothelial function (Hodgson et al., 2013). Experimental studies suggest that catechins may stabilize cardiac electrophysiology and reduce susceptibility to arrhythmias induced by ischemia-reperfusion injury.

6. ***Dracaena arborea***

Although less studied than the examples above, *Dracaena arborea* contains flavonoids, saponins, glycosides, and terpenoids, which have been reported to exert anti-inflammatory, antioxidant, and potential cardioprotective effects (Sun et al., 2019). These phytochemicals may influence ion channels, stabilize myocardial membranes, and modulate conduction, providing the rationale for investigating its antiarrhythmic activity in isolated heart models.

Medicinal plants continue to serve as valuable sources of cardioprotective and antiarrhythmic compounds. Through mechanisms such as ion channel modulation, antioxidant activity, anti-inflammatory effects, and regulation of autonomic tone, plant-derived phytochemicals can influence cardiac rhythm and protect myocardial tissue. Studies on plants like Digitalis purpurea, Rauwolfia serpentina, and Crataegus species provide precedence for exploring lesser-studied plants, including *Dracaena arborea*, in the search for safer and accessible antiarrhythmic agents.

1.8 The Plant: Dracaena Arborea

1.8.1 Taxonomy and botanical description

Dracaena arborea is a perennial plant belonging to the family **Asparagaceae**, widely distributed in West and Central Africa. Its taxonomy is summarized as follows:

- **Kingdom:** Plantae
- **Phylum:** Tracheophyta
- **Class:** Liliopsida
- **Order:** Asparagales
- **Family:** Asparagaceae
- **Genus:** *Dracaena*
- **Species:** *Dracaena arborea*

The plant is commonly referred to as the “tree dracaena” and is recognized for its erect woody stem and slender branches. It may grow up to 5–10 meters in height under natural conditions. The leaves are linear-lanceolate, arranged alternately along the stem, and possess a glossy green

appearance. The flowers are small, fragrant, and typically appear in clusters, producing berries upon maturation. Morphological features such as leaf arrangement, stem texture, and inflorescence pattern distinguish D. *arborea* from other species within the genus.

1.8.2 Ethnomedicinal uses

Dracaena arborea has a long history of traditional use among indigenous populations for the management of various ailments. In West African traditional medicine, the plant is employed to treat cardiovascular disorders, particularly hypertension and palpitations, which suggests a potential influence on cardiac rhythm. Additionally, it is used for inflammatory conditions, sexual dysfunction, and general debility. Preparations are typically made from the stem bark or leaves, either as decoctions, infusions, or macerated extracts.

Several ethnobotanical surveys report its use in combination with other medicinal plants for treating systemic disorders, highlighting its role in multi-targeted therapy. Traditional healers attribute its efficacy to the plant's "tonic" properties, which are believed to strengthen the heart, enhance vitality, and restore overall physiological balance. The ethnomedicinal background provides a rationale for pharmacological investigation, particularly in exploring its potential antiarrhythmic and cardioprotective effects.

1.8.3 Phytochemical constituents

Phytochemical studies of *Dracaena arborea* have revealed the presence of several bioactive compounds that may contribute to its pharmacological actions. Key constituents identified include:

- **Flavonoids:** Known for their antioxidant, anti-inflammatory, and membrane-stabilizing properties, flavonoids may modulate cardiac ion channels and influence action potential duration.

- **Saponins:** These compounds are reported to stabilize cell membranes, enhance contractility, and exert cardioprotective effects.
- **Glycosides:** Cardioactive glycosides may improve myocardial contractility and regulate heart rhythm.
- **Terpenoids:** Terpenoids have antioxidant and anti-inflammatory properties that may protect myocardial tissue from oxidative stress-induced damage.

These phytochemicals act synergistically to produce multiple cardiovascular effects, supporting the traditional use of D. *arborea* in heart-related ailments. The diverse phytochemical profile also positions the plant as a potential source of novel bioactive molecules for antiarrhythmic drug development.

1.8.4 Reported pharmacological properties

Experimental studies on *Dracaena arborea* remain limited; however, several pharmacological activities have been documented:

1. **Cardiovascular effects**

   Preliminary studies suggest that extracts of D. *arborea* may influence heart rate and contractility, supporting its traditional use for palpitations and hypertension. These effects are thought to arise from modulation of ion channels and enhancement of myocardial membrane stability.

2. **Antioxidant and anti-inflammatory effects**

   The presence of flavonoids and saponins contributes to the plant's ability to scavenge free radicals and inhibit pro-inflammatory mediators. This property is particularly

relevant in cardiovascular pharmacology, as oxidative stress and inflammation play a critical role in arrhythmogenesis and myocardial injury.

3. **Cytoprotective activity**

Some studies indicate that D. *arborea* extracts can protect tissues from chemical-induced damage, suggesting potential anti-apoptotic mechanisms that may safeguard cardiomyocytes.

4. **Other pharmacological actions**

Ethnobotanical reports and preliminary studies suggest potential effects on fertility, sexual function, and general systemic tonic activity. These ancillary effects may contribute indirectly to cardiovascular health by improving overall physiological resilience.

Collectively, the documented phytochemicals and pharmacological properties of *Dracaena arborea* provide a strong rationale for investigating its antiarrhythmic activity using experimental models such as isolated rat atria and perfused rabbit hearts. Such studies may uncover new plant-based strategies for managing cardiac rhythm disturbances and supporting traditional medicine practices with scientific validation.

Dracaena arborea is a medicinal plant with ethnopharmacological relevance in cardiovascular health. Its taxonomy, botanical features, traditional uses, and bioactive constituents lay the foundation for scientific evaluation of its pharmacological effects. Evidence of antioxidant, anti-inflammatory, and potential cardioprotective actions highlights the plant's promise as a source of novel antiarrhythmic agents. Further experimental studies are warranted to explore its mechanism of action and validate its therapeutic potential.

1.9 Rationale for the study

Cardiovascular diseases, particularly arrhythmias, remain a significant cause of morbidity and mortality worldwide. Despite advances in pharmacotherapy, conventional antiarrhythmic drugs are associated with limitations including narrow therapeutic indices, organ toxicity, proarrhythmic risks, and high cost (Nattel, 2017). These challenges are particularly pronounced in developing countries such as Nigeria, where access to specialist cardiac care and modern pharmacological agents is often limited. Consequently, there is an urgent need for alternative, safe, and effective therapies that can complement or substitute existing treatments for arrhythmias.

Traditional medicinal plants have historically played a vital role in managing cardiovascular disorders, providing a readily accessible source of bioactive compounds. *Dracaena arborea*, a perennial plant widely distributed in West and Central Africa, has been used ethnomedicinally to manage conditions such as hypertension, palpitations, and inflammatory disorders (Beppe et al., 2019). Phytochemical investigations have revealed the presence of flavonoids, saponins, glycosides, and terpenoids—compounds that are known to exert antioxidant, anti-inflammatory, and cardioprotective effects. These properties suggest that the plant may influence cardiac excitability, stabilize myocardial membranes, and modulate conduction, making it a promising candidate for antiarrhythmic evaluation.

While the ethnomedicinal use of *Dracaena arborea* for cardiovascular health is well documented, there is limited scientific evidence validating its effects on cardiac rhythm. Experimental pharmacology provides an opportunity to investigate its pharmacological potential under controlled conditions. In vitro models such as isolated rat atrial preparations (organ bath) and Langendorff-perfused rabbit hearts allow precise assessment of the effects of

plant extracts on contractility, conduction, and arrhythmogenesis without the confounding influence of systemic variables (Curtis and Walker, 2018).

By evaluating the antiarrhythmic effect of *Dracaena arborea* using these models, this study seeks to bridge the gap between traditional knowledge and modern scientific validation. Such research could provide evidence-based support for the safe use of D. *arborea* in managing arrhythmias, potentially leading to the development of plant-derived therapeutic agents that are affordable, effective, and accessible to populations in resource-limited settings. Additionally, findings from this study may stimulate further research into the isolation and characterization of active compounds within the plant, contributing to drug discovery and cardiovascular pharmacology.

In summary, the rationale for this study is grounded in the high prevalence of arrhythmias, the limitations of current pharmacological therapy, and the therapeutic potential of *Dracaena arborea* as a safe, accessible, and scientifically promising antiarrhythmic agent. This research aligns with global and local priorities to explore herbal remedies for cardiovascular disorders and provides a foundation for evidence-based integration of traditional medicine into modern healthcare.

1.10 Aim and Objectives of The Study

1.10.1 Aim

The aim of this study is to evaluate the antiarrhythmic effect of the methanolic extract of *Dracaena arborea* on isolated rat atria and perfused rabbit heart.

1.10.2 Specific objectives

1. To extract and prepare the methanolic extract of *Dracaena arborea*.

2. To assess the effect of the extract on the contractile activity of isolated rat atrial tissue using the organ bath technique.

3. To evaluate the antiarrhythmic effect of the extract on the perfused rabbit heart using the Langendorff apparatus.

4. To compare the observed effects of the extract with a standard antiarrhythmic drug (e.g., quinidine or propranolol).

CHAPTER TWO

MATERIALS AND METHODS

2.1 Materials

This study utilized a variety of materials, categorized into biological specimens, laboratory glassware, and general laboratory supplies. These materials were essential for ensuring accuracy, efficiency, and reliability in the experimental procedures.

Biological materials

The primary biological material used in this study was the thoracic aorta obtained from Wistar rats. This tissue was isolated and prepared to assess vascular responses. Additionally, a gas of 100% was used to aerate the Ringer locke solution, ensuring proper oxygenation and maintaining physiological pH throughout the experiment.

Laboratory glassware

Several types of glassware were required for solution preparation, sample handling, and experimental procedures

a. Beakers (50 mL – 500 mL) Used for mixing and storing liquid solutions.
b. Conical and Volumetric Flasks (100 mL – 500 mL) Used for precise solution preparation.
c. Petri Dishes Used to hold tissue samples before mounting in the organ bath.
d. Measuring Cylinders (10 mL – 500 mL) Used to measure liquid volumes accurately.
e. Glass Funnels and Filter Paper Used for filtering plant extracts and other solutions.

General laboratory supplies

To maintain sterility, safety, and precision, various laboratory supplies were utilized

a. Disposable Gloves Worn to prevent contamination while handling biological samples and chemicals.
b. Lab Coats and Safety Goggles Provided protection against chemical spills and biological exposure.
c. Tissue Papers and Wipes Used for cleaning work surfaces and drying equipment.
d. Digital Weighing Balance Used to measure plant extracts and chemical reagents accurately.

2.1.1 Apparatus

Various laboratory instruments and equipment were utilized in this study to facilitate plant extraction and tissue preparation, experimental setup, and data recording. These apparatus were essential for ensuring precision, maintaining controlled conditions, and obtaining accurate measurements and they include;

Soxhlet Apparatus

The Soxhlet apparatus, utilized with distilled water, facilitated an effective and exhaustive extraction of bioactive compounds from the *Dracaena arborea* leaves. This method ensured continuous solvent recycling, thereby enhancing extraction efficiency and preserving heat-sensitive phytochemicals. The technique provides a high yield of active constituents essential for further phytochemical and pharmacological analyses (Okonkwo et al., 2020).

Organ bath system

a. Organ Bath (25–50 mL capacity) A chamber used to immerse isolated aortic rings in Krebs-Henseleit solution, ensuring physiological conditions for vascular response studies (Wenceslau et al., 2021).

b. Water Bath (37°C) Maintained the organ bath at body temperature (37°C) to preserve tissue viability (Mulvany and Halpern, 1977).

c. Oxygen gas (Carbogen Gas Delivery System) to oxygenate the physiological salt solution and maintain pH balance (Angus and Wright, 2000).

Data recording and measurement instruments

a. Isometric Force Transducer Converted mechanical tension changes in aortic tissue into electrical signals for analysis.

b. Data Acquisition System (Computer Software) Recorded and analysed vascular responses.

c. Physiograph Provided a real-time graphical representation of tissue contraction and relaxation.

Langendorff apparatus

Reservoir (Perfusate Reservoir)

Holds the physiological perfusion solution (e.g., Krebs–Henseleit buffer) that supplies nutrients and oxygen to the isolated heart. The reservoir is often maintained at 37°C to simulate normal body temperature (Bell, Mocanu, and Yellon, 2011).

Heater/water bath system

Maintains the perfusion solution and heart chamber at 37°C to mimic physiological temperature and ensure tissue viability (Liao, Podesser, and Lim, 2012).

Oxygenator

Continuously bubbles of oxygen gas through the perfusate to ensure oxygenation and maintain pH balance (Korvald, Elvenes, and Myrmel, 2000).

Peristaltic or pressure pump

Delivers the perfusate to the heart at a controlled rate or pressure. The system can operate in constant flow mode (using a peristaltic pump) or constant pressure mode (using a reservoir and regulator) depending on experimental needs (de Beer et al., 2019).

Thermostatically controlled perfusion chamber

Houses the isolated heart and collects the coronary effluent while maintaining the heart at physiological temperature and preventing desiccation (Liao et al., 2012).

Aortic cannula

Attached to the ascending aorta of the excised heart; it directs oxygenated perfusate retrogradely through the coronary arteries to ensure uniform perfusion (Bell et al., 2011).

Manometer or pressure transducer

Measures perfusion pressure or left ventricular pressure to assess cardiac contractility and coronary resistance (de Beer et al., 2019).

Venous outflow (coronary effluent collection system)

Collects the perfusate draining from the coronary sinus after circulating through the myocardium for biochemical or pharmacological analysis (Korvald et al., 2000).

Thermometer / temperature probe

Monitors the temperature of the perfusate and chamber to maintain constant physiological conditions (Liao et al., 2012).

Data acquisition system

Records physiological parameters such as heart rate, perfusion pressure, contractile force, and ECG in real time for analysis (Bell et al., 2011).

Tissue dissection and handling instruments

a. Forceps (Fine and Blunt-Tipped) Used for gripping and positioning aortic tissue during dissection and mounting.
b. Scalpel and Blades Used for precise excision of the aorta.
c. Scissors (Straight and Curved) Used for cutting and trimming connective tissue from the aortic rings.

Precision measurement equipment

a. Micropipettes (0.1–1000 µL) Used for accurate measurement and transfer of small liquid volumes, such as drug solutions and plant extracts.
b. Graduated Pipettes Used for precise liquid measurements and dilution of solutions.

2.1.2 Chemicals / drugs

Various chemicals and reagents were utilized in this study to prepare physiological solutions, induce vascular contractions, and assess the effects of *Dracaena arboreal* on isolated rat atrial and the whole rabbit heart. These substances played a critical role in ensuring the accuracy and reliability of the experimental results.

2.1.2.1 Chemicals for physiological salt solution preparation

Sodium chloride (NaCl)

Provides the principal extracellular cation (Na^+) and anion (Cl^-), essential for maintaining osmotic balance and resting membrane potential in tissues (Locke, 1896; Hainsworth, 1981).

Potassium chloride (KCl)

Supplies potassium ions (K^+), which are crucial for maintaining intracellular potential and regulating excitability in muscle and nerve tissues (Locke, 1896).

Calcium chloride ($CaCl_2$)

Ensures the availability of calcium ions (Ca^{2+}) necessary for muscle contraction and neurotransmitter release (Burn, 1952).

Sodium bicarbonate ($NaHCO_3$)

Acts as a buffering agent to maintain physiological pH (~7.4) in the solution and counteracts acid accumulation (Hainsworth, 1981).

Glucose ($C_6H_{12}O_6$)

Serves as an energy substrate for metabolic activity of isolated tissues or organs during in vitro experiments (Burn, 1952).

Distilled water

Acts as the solvent for dissolving all the salts and glucose, maintaining isotonicity with physiological fluids (Locke, 1896).

2.1.2.2 Typical composition (per liter of distilled water)

- NaCl: 9.0 g
- KCl: 0.42 g
- $CaCl_2$: 0.24 g
- $NaHCO_3$: 0.2 g
- Glucose: 1.0 g

2.1.3 Preparation of physiological salt solution

The Physiological Salt Solution (PSS) was prepared by dissolving specific chemical components in a sequential manner to ensure proper mixing and maintain a stable physiological environment for the isolated rat atria and rabbit heart. The solution was continuously aerated using oxygen gas to provide oxygenation.

Preparation procedure

1. Dissolution of main components

a. A measured volume of distilled water was transferred into a clean beaker.
b. The following chemicals were carefully added one after another, allowing each to completely dissolve before introducing the next
c. Sodium chloride (NaCl) – 9.0 g/L

d. Sodium bicarbonate ($NaHCO_3$) – 0.2 g/L

e. D-glucose – 1.0 g/L

f. Potassium chloride (KCl) – 0.42 g/L

g. Calcium chloride Dihydrate $CaCl_2.2H_2O$ 0.32 g/L

2. Preparation of calcium chloride solution

a. A separate beaker containing a small volume of distilled water was used to dissolve calcium chloride ($CaCl_2$) – 0.32 g/L.

b. This method was employed to prevent precipitation when combined with the other chemicals.

c. After ensuring complete dissolution, the calcium chloride solution was slowly poured into the main mixture while stirring continuously.

3. Aeration of the solution

To maintain optimal physiological conditions, oxygen gas was continuously bubbled through the solution to ensure proper oxygenation.

4. Storage and usage

a. The freshly prepared PSS was stored at room temperature and used immediately during the experiment.

b. When required for extended use, the solution was kept under continuous aeration to preserve its stability and effectiveness.

2.1.3.1 Plant extract

The extraction of *Dracaena arborea* was carried out using an aqueous extraction method in which equal volumes of water and methanol served as the solvent system to obtain the plant's bioactive compounds (Wankeu-Nya et al., 2014). This method ensures efficient isolation of active constituents while preserving their stability and biological activity for subsequent experimental applications (Nguelefack et al., 2019).

2.1.3.2 Collection and authentication of plant material

The leaves of *Dracaena arborea* were collected from a reliable local source and authenticated by a qualified botanist to confirm their taxonomic identity (Wankeu-Nya et al., 2014). Prior to extraction, the leaves were thoroughly washed with clean water to remove dust, debris, and other unwanted impurities, ensuring the purity of the plant material for subsequent experimental procedures (Ilodibia et al., 2015).

2.1.3.3 Drying and grinding

The cleaned leaves of *Dracaena arborea* were air-dried at room temperature in a well-ventilated area, protected from direct sunlight to prevent degradation of thermolabile bioactive compounds (Ilodibia et al., 2015). After complete drying, the leaves were ground into a fine powder using a mechanical grinder to increase the surface area for efficient solvent extraction (Nguelefack et al., 2019). The powdered plant material was then stored in an airtight container to prevent moisture absorption and preserve its phytochemical integrity prior to extraction (Wankeu-Nya et al., 2014).

2.1.3.4 Extraction procedure and storage of the extract

A measured quantity of the powdered *Dracaena arborea* leaves was extracted with distilled water using a Soxhlet apparatus, following a predetermined ratio to ensure efficient extraction of bioactive compounds (Nguelefack et al., 2019).

During extraction, the distilled water continuously refluxed over the plant material, ensuring thorough contact and effective isolation of active constituents (Wankeu-Nya et al., 2014). After the extraction period, the mixture was filtered through Whatman filter paper to separate the plant residues from the aqueous extract (Ilodibia et al., 2015). The filtrate was concentrated by evaporation in a drying oven to remove excess water, yielding the crude aqueous extract of *Dracaena arborea* (Nguelefack et al., 2019).

2.1.3.5 Storage of the extract

The crude extract was stored in a drying oven to remove any remaining moisture and to preserve its stability until required for experimentation (Ilodibia et al., 2015). When needed for the experiment, a specific quantity of the dried extract was weighed and dissolved in an appropriate volume of distilled water to prepare the test solutions (Nguelefack et al., 2019).

2.2 Preparation of *dracaena arborea* extract solution

The *Dracaena arboreal* extract solution was prepared by dissolving a specific amount of the dried extract in distilled water to obtain the required concentrations for the experiment.

Preparation procedure

1. **Extract weighing**

A precise digital balance was used to measure 1.0 g of the dried *Dracaena arborea* extract with high accuracy to ensure consistency in concentration and reproducibility (Nguelefack et al., 2019).

2. **Dissolution in distilled water**

The 1.0 g of extract was dissolved in 10 mL of distilled water to prepare a stock solution. The mixture was stirred continuously until complete dissolution was achieved, producing a homogeneous solution suitable for dilution (Ilodibia et al., 2015).

3. **Formulating various concentrations**

Serial dilutions of the stock solution were prepared with distilled water to obtain working concentrations of 50 mg/mL and 100 mg/mL. This was done by combining measured volumes of the stock solution with precise quantities of distilled water to achieve the desired concentrations (Wankeu-Nya et al., 2014).

4. **Volume measurement**

For each experimental concentration, exact volumes—0.05 mL and 0.1 mL of the 50 mg/mL solution, and 0.1 mL, 0.2 mL, and 0.4 mL of the 100 mg/mL solution—were accurately measured using a micropipette to ensure uniformity and precision across all trials (Nguelefack et al., 2019)

5. **Storage and use**

6. Finally, the prepared extract solutions were stored at room temperature and utilized immediately to maintain the stability and bioactivity of the compounds (Omoya and Oyebola, 2019).

2.3 Experimental Animals

1. Species and selection

Wistar rats were chosen for this research because their cardiovascular responses are well-documented and widely used as a standard model in such studies (National Research Council, 2011; Sengupta, 2013).

2. Animal characteristics

The study utilized Wistar rats of both sexes, with an average body weight ranging from 200 to 300 g and rabbits weighing an average of 1250 g to 2250 g. This selection criteria help ensure uniformity in physiological responses, allowing for meaningful comparisons across different studies (National Research Council, 2011).

3. Housing and care

The animals were housed in standard laboratory cages with unlimited access to food and water. They were maintained under rigorously controlled conditions—including a 12-hour light/dark cycle, stable room temperature, and proper ventilation—to safeguard their well-being throughout the duration of the study (National Research Council, 2011).

4. Ethical considerations

All animal procedures were performed in strict accordance with established ethical guidelines for laboratory animal care. This adherence to protocols, as specified in the NIH Guide for the Care and Use of Laboratory Animals, ensured that the rats experienced minimal discomfort and were treated humanely (National Research Council, 2011).

2.4 Method

2.4.1 Experimental procedure

This experiment was conducted to investigate the effects of *Dracaena arboreal* extract on isolated rat atria tissue. The procedures followed are outlined below.

1. **Animal selection and preparation**

   Adult Wistar rats weighing between 270±30g and rabbits weighing an average of 2.125kg±0.125kg were chosen for this study because their cardiovascular responses are well characterized and they serve as a standard model in vascular research (National Research Council, 2011; Sengupta, 2013).

2. **Tissue preparation for isolated heart atria**

   Adult rats were anesthetized according to ethical guidelines, and the hearts were excised and immediately placed in cold, oxygenated Ringer-Locke maintained at 37°C (Bell et al., 2011). The atria were dissected free of connective tissue and mounted in an organ bath between a stationary hook and a force transducer using fine silk sutures (Mulvany and Halpern, 1977). The tissue was submerged in oxygenated Ringer-Locke solution and an initial resting tension of 0.5–1.0 g was applied (Furchgott and Zawadzki, 1980). The

preparation was equilibrated for 30–45 minutes with periodic buffer changes before baseline contractile recordings or pharmacological testing were conducted (Vanhoutte et al., 1981).

3. **Application of extract**

After stabilization, the aortic rings were exposed to cumulative concentrations of *Dracaena arboreal* extract—specifically, 0.05 mL and 0.1 mL of the 50 mg/mL solution, and 0.1 mL, 0.2 mL, and 0.4 mL of the 100 mg/mL solution. The extract solution was added directly into the organ bath. The resulting vascular responses were recorded and subsequently analysed.

2.4.2 Pharmacological agents used

Calcium chloride

Calcium ions (Ca^{2+}) play a crucial role in cardiac excitation–contraction coupling. The addition of calcium chloride ($CaCl_2$) to the organ bath increases the extracellular calcium concentration, thereby enhancing the contractile force of the isolated atrial tissue (Bers, 2002).

An elevated Ca^{2+} gradient across the sarcolemma promotes greater calcium influx through L-type calcium channels during depolarization (Bers, 2002; Katz, 2011). The increased intracellular calcium then binds to troponin C, facilitating actin–myosin cross-bridge cycling and resulting in a positive inotropic effect—manifested as stronger atrial contractions (Rang et al., 2016).

Additionally, higher Ca^{2+} levels can increase spontaneous firing rate in pacemaker cells by enhancing the rate of depolarization and reducing the threshold for action potential

initiation (Guyton and Hall, 2021). However, excessive extracellular calcium may lead to decreased relaxation, arrhythmogenic activity, or diastolic contracture, due to calcium overload in the myocytes (Katzung et al., 2018).

In summary, moderate increases in $CaCl_2$ concentration produce increased amplitude and frequency of atrial contractions, while excessive calcium concentrations may impair relaxation and alter rhythm. Different concentrations of calcium chloride was added (0.2mM, 0.5mM, 1mM, 2mM and 4mM).

Adrenaline

Adrenaline (epinephrine) exerts a positive chronotropic (increased heart rate) and positive inotropic (increased contractile force) effect on the isolated atrial tissue. These effects are mediated primarily through the activation of β_1-adrenergic receptors located on cardiac myocytes (Bers, 2002). Upon binding, adrenaline stimulates adenylyl cyclase, leading to an increase in intracellular cyclic adenosine monophosphate (cAMP), which in turn activates protein kinase A (PKA) (Katzung et al., 2018).

PKA phosphorylates L-type calcium channels, enhancing Ca^{2+} influx during depolarization and thereby increasing the availability of calcium for excitation–contraction coupling (Bers, 2002). This results in stronger myocardial contractions (positive inotropy). PKA also accelerates the reuptake of calcium into the sarcoplasmic reticulum via phospholamban phosphorylation, which shortens relaxation time and contributes to an increased rate of contraction (positive lusitropy) (Bers, 2002; Katz, 2011).

In addition, adrenaline increases the rate of spontaneous depolarization of pacemaker cells in the sinoatrial node, leading to an increase in heart rate (positive chronotropy) (Rang et al., 2016). In isolated atrial preparations, these effects manifest as increased amplitude and

frequency of atrial contractions, observable through enhanced tension development and faster beating rate in organ bath recordings (Vanhoutte et al., 1981). Different concentrations of adrenaline was added in 0.1mL and 0.3mL. 5.4E-8µg/mL, 1.64E-7µg/mL, 5.4E-7µg/mL, 1.64E-6µg/mL, 5.4E-6µg/mL, 1.64E-5µg/mL, 5.4E-5mg/mL, 1.64E-4 mg/mL.

Atropine

Atropine is a competitive antagonist of muscarinic acetylcholine receptors (M_2 subtype) located in the sinoatrial (SA) node and atrial myocardium (Katzung et al., 2018). Under normal physiological conditions, acetylcholine released from parasympathetic vagal fibers binds to these receptors, activating Gi-proteins that inhibit adenylyl cyclase, reduce cAMP levels, and consequently decrease heart rate and contractility (Rang et al., 2016).

By blocking these receptors, atropine inhibits parasympathetic (vagal) tone, leading to increased heart rate (positive chronotropic effect) and enhanced conduction through the atrioventricular (AV) node (Guyton and Hall, 2021). In isolated atrial preparations, this manifests as an increase in contraction rate and sometimes a slight rise in contractile force, since intrinsic pacemaker activity becomes unopposed by acetylcholine-mediated inhibition (Katz, 2011).

When atropine is applied after acetylcholine, it reverses the negative chronotropic and inotropic effects produced by acetylcholine, confirming its role as a muscarinic receptor blocker (Goodman and Gilman, 2018). 1.5E-5 µg/mL of atropine was added.

Atenolol

Atenolol is a selective β_1-adrenergic receptor antagonist that primarily acts on cardiac tissue (Katzung et al., 2018). In the heart, β_1 receptors mediate sympathetic stimulation by norepinephrine and epinephrine, leading to increased cyclic adenosine monophosphate (cAMP) levels, enhanced calcium influx, and consequently increased heart rate (positive chronotropy) and contractile force (positive inotropy) (Rang et al., 2016).

By competitively blocking these β_1 receptors, atenolol reduces the effects of endogenous catecholamines, resulting in a decrease in heart rate and contractility (negative chronotropic and inotropic effects) (Goodman and Gilman, 2018). In isolated atrial preparations, atenolol typically causes a reduction in the frequency and amplitude of contractions, especially if the tissue has been previously stimulated by adrenaline or is under sympathetic drive (Guyton and Hall, 2021).

Thus, atenolol serves as an important pharmacological tool to demonstrate β_1-adrenergic blockade, showing the inhibitory control of sympathetic stimulation on cardiac function (Katz, 2011). 1.5E-6 µg/mL of atenolol was added.

2.5 Statistical Analysis

All data were expressed as mean ± standard error of the mean (SEM) of at least three independent experiments. Differences between groups were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test for multiple comparisons. A p-value of <0.05 was considered statistically significant. Graphical representations and statistical analyses were performed using GraphPad Prism version 9.0 (GraphPad Software, San Diego, CA, USA).

CHAPTER THREE

RESULTS

The extract of *Dracaena arborea* exhibited a concentration-dependent suppression of induced arrhythmic activity in isolated cardiac tissues. At lower concentrations (0.25-1 mg/mL), the extract produced a mild stabilization of the rhythm with slight prolongation of the action potential duration, while higher concentrations (2-4 mg/mL) caused a marked reduction in ectopic beats and spontaneous irregular contractions (Table 3.1) and (fig 3.1).

At the maximal concentration tested (4 mg/mL), the extract completely abolished the arrhythmic discharges induced by adrenaline or calcium chloride, an effect that was reversed upon washing the tissue with drug-free Locke Ringer solution.

Pretreatment with Atenolol (1.5×10^{-6} M) or atropine (3×10^{-6} M) did not significantly alter the anti-arrhythmic action of the extract, suggesting that its effect is not mediated through β-adrenergic or muscarinic receptors.

Table 3.1: The effects of *Dracaena arborea* hydroalcoholic extract on the spontaneously beating rat atria in the absence and presence of atropine.

Conc (mg/ml)	**Rate of contraction (mm/min) ± SEM**		**Force of contraction (cm) ± SEM**	
	Extract alone	**Extract + Atropine**	**Extract alone**	**Extract + Atropine**
0.25	32.00± 5.28	37.00 ± 3.16	3.29 ± 0.11	3.33 ± 0.12
0.5	36.00 ± 4.82	42.00 ± 3.63	3.05 ± 0.07	3.24 ± 0.14
1	38.00 ± 3.99	41.00 ± 4.18	2.88 ± 0.10	3.13 ± 0.17
2	37.00 ± 5.01	42.00 ± 4.85	2.39 ± 0.11	2.88 ± 0.13
4	38.00 ± 5.64	44.00 ± 5.70	0.10 ± 0.01	2.35 ± 0.19

Table 3.2: Effect of adrenaline on the rate of contraction of the spontaneously beating rat atria, in the absence and presence of *Dracaena arborea* hydroalcoholic extract and atenolol

Concentration (M)	**Rate of contraction (mm/min)**			
	Adrenaline alone	**Adrenaline + Extract**	**Adrenaline + Atenolol**	**Adrenaline +Extract + Atenolol**
5.4×10^{-8}	57.00 ± 2.06	44.00 ± 1.97	45.00 ± 2.23	47.00 ± 2.32
1.64×10^{-7}	55.00 ± 2.03	44.00 ± 2.48	48.00 ± 2.19	49.00 ± 2.71
5.4×10^{-7}	55.00 ± 1.32	48.00 ± 2.51	51.00 ± 2.28	51.00 ± 2.48
1.64×10^{-6}	57.00 ± 2.31	48.00 ± 1.94	53.00 ± 2.24	54.00 ± 2.48
5.40×10^{-6}	58.00 ± 2.93	51.00 ± 2.67	53.00 ± 2.28	55.00 ± 2.33
1.64×10^{-5}	56.00 ± 3.10	49.00 ± 2.14	55.00 ± 1.51	55.00 ± 2.51
5.40×10^{-5}	59.00 ± 1.23	53.00 ± 2.16	57.00 ± 1.83	56.00 ± 1.86
1.64×10^{-4}	60.00 ± 1.41	57.00 ± 1.69	60.00 ± 1.67	60.00 ± 1.51

Table 3.3: Effect of adrenaline on the contractile force of the spontaneously beating rat atria, in the absence and presence *Dracaena arborea* of hydroalcoholic extract and atenolol

Concentration (M)	**Force of Contraction (cm)**			
	Adrenaline alone	**Adrenaline + Extract**	**Adrenaline + Atenolol**	**Adrenaline + Extract + Atenolol**
5.4×10^{-8}	2.44 ± 0.07	2.51 ± 0.06	2.71 ± 0.04	2.58 ± 0.07
1.64×10^{-7}	2.58 ± 0.08	2.43 ± 0.05	2.63 ± 0.05	2.58 ± 0.09
5.4×10^{-7}	2.68 ± 0.11	2.42 ± 0.05	2.52 ± 0.08	2.43 ± 0.08
1.64×10^{-6}	2.82 ± 0.11	2.27 ± 0.06	2.48 ± 0.06	2.35 ± 0.08
5.4×10^{-6}	2.92 ± 0.10	2.17 ± 0.05	2.33 ± 0.04	2.24 ± 0.003
1.64×10^{-5}	3.07 ± 0.10	2.14 ± 0.05	2.28 ± 0.06	2.44 ± 0.27
5.4×10^{-5}	3.16 ± 0.08	2.07 ± 0.07	2.26 ± 0.06	2.01 ± 0.03
1.64×10^{-4}	3.36 ± 0.10	1.89 ± 0.06	2.13 ± 0.05	1.93 ± 0.06

Table 3.4: The effects of calcium chloride on the rate and force of contraction of the spontaneously beating rat atria in the absence and presence of *Dracaena arborea* hydroalcoholic extract

Concentration (mM)	**Heart Rate (mm/min) ± SEM**		**Force of contraction (cm) ± SEM**	
	$CaCl_2$ alone	**$CaCl_2$ + Extract**	**$CaCl_2$ alone**	**$CaCl_2$ + Extract**
0.25	50.00 ± 2.46	52.00 ± 3.32	2.61 ± 0.05	2.76 ± 0.07
0.5	53.00 ± 1.11	56.00 ± 4.18	2.70 ± 0.06	2.67 ± 0.06
1	56.00 ± 0.61	54.00 ± 1.05	2.84 ± 0.06	2.52 ± 0.07
2	57.00 ± 2.46	59.00 ± 1.80	2.98 ± 0.05	2.33 ± 0.08
4	62.00 ± 1.41	60.00 ± 0.00	3.26 ± 0.04	2.15 ± 0.08

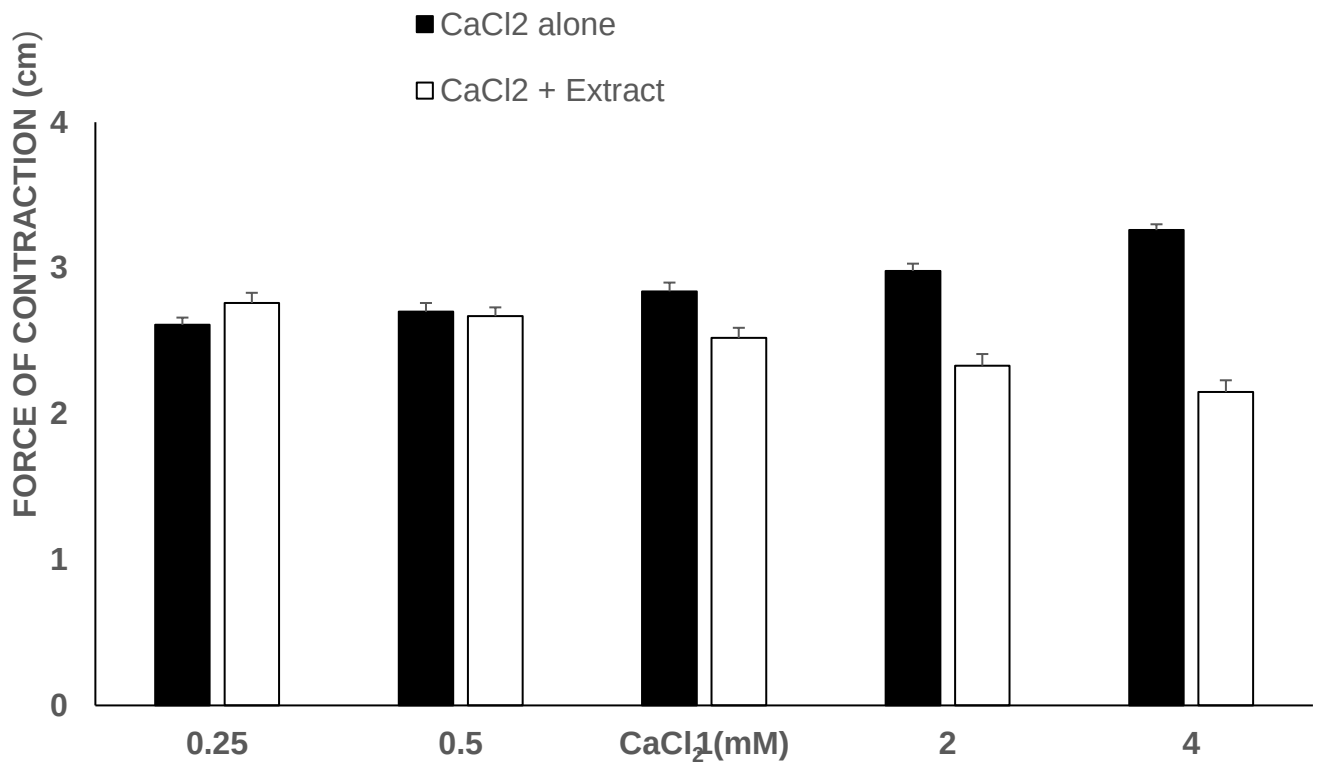

Fig. 3.2. The effect of calcium chloride on the force of contraction of the spontaneously beating rat atria in the absence and presence of *Dracaena arborea* hydroalcoholic extract

Table 3.5: The effect of adrenaline on the heart rate and force of contraction in the presence of plant extract and atenolol

	Heart rate (mm/min)				**Force of Contraction**			
Concentration (M)	**Adr alone**	**Adr + Extract**	**Adr + Atenolol**	**Adr+Extr+ Atenolol**	**Adr Alone**	**Adr + Extract**	**Adr + Atenolol**	**Adr+Extr+ Atenolol**
5.4×10^{-8}	57 ± 2.06	44.00 ± 1.97	45.00 ± 2.23	47.00 ± 2.32	2.44 ± 0.07	2.51 ± 0.06	2.71 ± 0.04	2.58 ± 0.07
1.64×10^{-7}	55 ± 2.03	44.00 ± 2.48	48.00 ± 2.19	49.00 ± 2.71	2.58 ± 0.08	2.43 ± 0.05	2.63 ± 0.05	2.58 ± 0.09
5.4×10^{-7}	55 ± 1.32	48.00 ± 2.51	51.00 ± 2.28	51.00 ± 2.48	2.68 ± 0.11	2.42 ± 0.05	2.52 ± 0.08	2.43 ± 0.08
1.64×10^{-6}	57 ± 2.31	48.00 ± 1.94	53.00 ± 2.24	54.00 ± 2.48	2.82 ± 0.11	2.27 ± 0.06	2.48 ± 0.06	2.35 ± 0.08
5.4×10^{-6}	58 ± 2.93	51.00 ± 2.67	53.00 ± 2.28	55.00 ± 2.33	2.92 ± 0.10	2.17 ± 0.05	2.33 ± 0.04	2.24 ± 0.003
1.64×10^{-5}	56 ± 3.10	49.00 ± 2.14	55.00 ± 1.51	55.00 ± 2.51	3.07 ± 0.10	2.14 ± 0.05	2.28 ± 0.06	2.44 ± 0.27
5.4×10^{-5}	59 ± 1.23	53.00 ± 2.16	57.00 ± 1.83	56.00 ± 1.86	3.16 ± 0.08	2.07 ± 0.07	2.26 ± 0.06	2.01 ± 0.03
1.64×10^{-4}	60 ± 1.41	57.00 ± 1.69	60.00 ± 1.67	60.00 ± 1.51	3.36 ± 0.10	1.89 ± 0.06	2.13 ± 0.05	1.93 ± 0.06

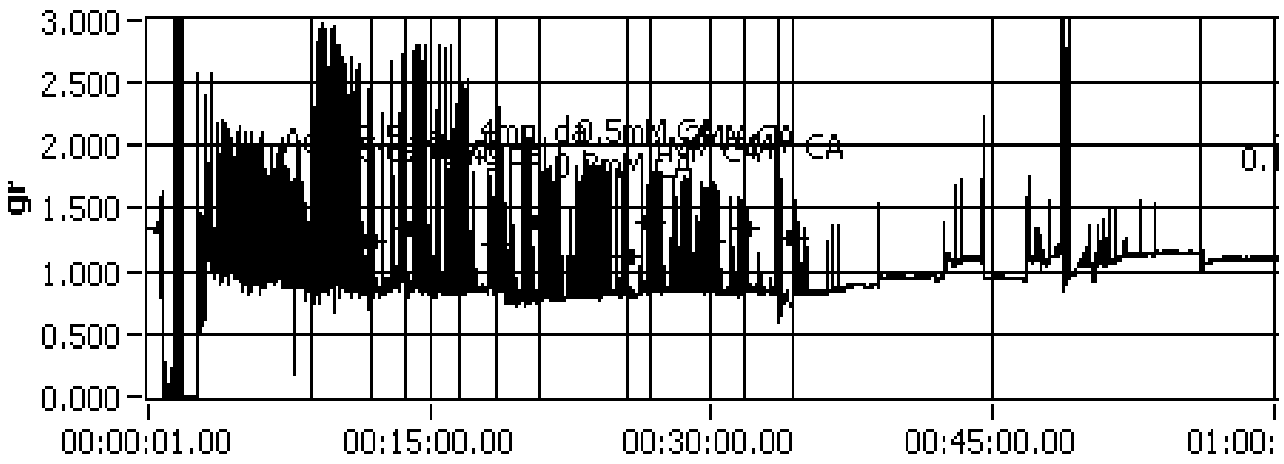

Fig 3: Representative tracing showing the direct effect of *Dracaena arborea* hydroalcoholic extract on the isolated perfused rabbit heart

CHAPTER FOUR
DISCUSSION

This study investigated the effect of *Dracaena arborea* hydroalcoholic extract on spontaneously beating rat atria and isolated perfused rabbit heart preparations, with particular emphasis on its influence on heart rate, force of contraction, and induced arrhythmic activity. The findings demonstrate that the extract possesses significant anti-arrhythmic properties, evident from its concentration-dependent suppression of arrhythmias induced by adrenaline and calcium chloride.

The results obtained from the spontaneously beating rat atria revealed that *Dracaena arborea* hydroalcoholic extract produced a concentration-dependent modulation of cardiac activity. At lower concentrations (0.25–1 mg/mL), the extract caused only mild changes in heart rate and force of contraction, accompanied by a stabilization of rhythm and slight prolongation of action potential duration. This suggests an initial cardiostabilizing effect rather than a profound depressant action.

At higher concentrations (2–4 mg/mL), a marked reduction in force of contraction was observed, particularly evident at 4 mg/mL where a near-complete suppression of contractile force occurred. This negative inotropic effect may be attributed to reduced intracellular calcium availability or interference with excitation–contraction coupling. Despite this reduction in force, heart rate was not drastically suppressed, indicating that the extract preferentially affects myocardial contractility over pacemaker activity.

The observation that atropine did not significantly alter the effects of the extract on either heart rate or force of contraction suggests that the action of *Dracaena arborea* is not mediated via muscarinic cholinergic pathways. This further supports a direct myocardial action rather than an indirect autonomic mechanism.

The extract exhibited a pronounced ability to suppress arrhythmias induced by both adrenaline and calcium chloride, with complete abolition of arrhythmic discharges at the

highest concentration tested (4 mg/mL). Importantly, this effect was reversible upon washing with drug-free Locke Ringer solution, indicating that the extract does not cause irreversible myocardial damage.

Pretreatment with atenolol, a selective β_1-adrenergic blocker, did not significantly modify the anti-arrhythmic effect of the extract. This finding strongly suggests that the mechanism of action is independent of β-adrenergic receptor blockade. Similarly, the lack of influence of atropine excludes parasympathetic involvement.

Based on these observations, the anti-arrhythmic effect of *Dracaena arborea* may be mediated through:

- **Inhibition of calcium influx** via L-type calcium channels, as evidenced by attenuation of calcium chloride–induced increases in contractile force.
- **Stabilization of cardiac membrane excitability**, possibly through modulation of sodium or potassium channels, resulting in reduced ectopic activity and prolonged action potential duration.
- **Reduction in intracellular calcium overload**, which is a known trigger for arrhythmogenesis, especially in catecholamine- and calcium-induced arrhythmias.

These mechanisms are consistent with the ability of the extract to suppress spontaneous irregular contractions and ectopic beats without reliance on autonomic receptor pathways.

The demonstrated suppression of arrhythmic activity suggests that *Dracaena arborea* hydroalcoholic extract possesses potential therapeutic relevance in the management of cardiac arrhythmias. Its ability to counteract adrenaline-induced arrhythmias indicates possible usefulness in stress- or catecholamine-mediated arrhythmic conditions. Additionally, its effectiveness against calcium chloride–induced arrhythmias highlight a role in conditions associated with calcium overload.

However, the pronounced negative inotropic effect observed at higher concentrations suggests that careful dose consideration would be essential to avoid excessive depression of myocardial contractility. This balance between anti-arrhythmic efficacy and cardiac depressant effects is a critical consideration in clinical application.

Conventional anti-arrhythmic drugs, such as β-blockers and calcium channel blockers, exert their effects through specific receptor-mediated or ion channel–specific mechanisms. In contrast, *Dracaena arborea* extract appears to exert a broader, receptor-independent cardiostabilizing action.

Unlike atenolol, which reduces heart rate and contractility primarily through β_1-adrenergic blockade, the extract maintained its anti-arrhythmic effect even in the presence of atenolol. This suggests a mechanism distinct from classical β-blockade. Similarly, its effects resemble those of calcium channel blockers in reducing calcium-induced contractility, yet without exclusive reliance on calcium antagonism.

Thus, *Dracaena arborea* may represent a phytochemical alternative with multi-target actions, potentially offering advantages in cases where conventional anti-arrhythmic agents are ineffective or contraindicated.

The findings of this study provide experimental evidence supporting the traditional medicinal use of *Dracaena arborea* in cardiovascular disorders. The demonstrated anti-arrhythmic activity, coupled with reversible effects and receptor-independent mechanisms, underscores the pharmacological significance of the plant.

Future studies should focus on:

- Isolation and characterization of the active phytochemical constituents responsible for the observed effects.
- Detailed electrophysiological studies to elucidate specific ion channel interactions.
- In vivo investigations to assess safety, efficacy, and therapeutic index.

- Toxicological profiling to determine long-term cardiovascular safety.

In conclusion, *Dracaena arborea* hydroalcoholic extract exhibits significant concentration-dependent anti-arrhythmic activity in isolated cardiac preparations, mediated through direct myocardial actions rather than autonomic receptor modulation. These findings justify further investigation into its potential development as a novel anti-arrhythmic agent.

CHAPTER FIVE

CONCLUSION

Based on the experimental findings of this study, it was concluded that the methanol stem bark extract of *Dracaena arborea* exhibits significant anti-arrhythmic properties. The extract produced a concentration modulation of cardiac activity, evidenced by its ability to regulate heart rate and improve the force of contraction in vitro. When compared with calcium chloride-induced arrhythmic responses, the extract demonstrated a protective effect, suggesting that its bioactive constituents may stabilize cardiac electrophysiology and prevent abnormal pacemaker activity. The observed cardioprotective effects provide a scientific basis for further investigation into *Dracaena arborea* as a promising natural source for developing plant-derived anti-arrhythmic agents.

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