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Case Study
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EVALUATION OF CARDIAC RESPONSES TO ADRENALINE AND PROPRANOLOL IN EXPERIMENTAL MODELS

C.MAHALAKSHMI[1], KAVIBHARATHI[1], V.V VENKATACHALAM*[1], SUNDERAJAN[2]

[1]Department of Pharmacology, Mohamed Sathak A J College of Pharmacy, Perumbakkam Main Rd, Sholinganallur, Chennai, Tamil Nadu 600119
[2]Principal, Mohamed Sathak A J College of Pharmacy, Perumbakkam Main Rd, Sholinganallur, Chennai, Tamil Nadu 600119

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***Corresponding Author**
V.V Venkatachalam

Abstract
The present study was undertaken to evaluate the cardiac effects of adrenaline, a β-adrenergic agonist, and propranolol, a non-selective β-adrenergic antagonist, using an isolated heart preparation. The primary objective was to investigate changes in heart rate and contractile force and to determine the nature of interaction between these drugs. Adrenaline was administered in graded concentrations, producing a dose-dependent increase in heart rate and contraction amplitude, indicating positive chronotropic and inotropic effects. Propranolol administration resulted in a significant reduction in cardiac activity, demonstrating effective β-receptor blockade. When adrenaline was administered in the presence of propranolol, the responses were markedly reduced, and a rightward shift in the dose-response curve was observed without a decrease in maximum response (Emax), confirming competitive antagonism. The findings of this study highlight the role of β-adrenergic receptors in cardiac regulation and support the therapeutic significance of β-blockers in managing cardiovascular disorders.

Keywords: *Adrenaline, Propranolol, β-adrenergic receptors, Isolated heart, Dose-response curve, Competitive antagonism, Chronotropic effect, Inotropic effect.*

INTRODUCTION

The cardiovascular system is tightly regulated by the autonomic nervous system, with sympathetic stimulation playing a crucial role in modulating heart rate, myocardial contractility, and conduction velocity. Among the key mediators of sympathetic activity, adrenaline (epinephrine) is a potent endogenous catecholamine that exerts its effects primarily through activation of β-adrenergic receptors in cardiac tissue. Activation of β_1-receptors leads to positive chronotropic, inotropic, and dromotropic effects, thereby increasing cardiac output and oxygen demand [1,2].

In contrast, propranolol is a non-selective β-adrenergic receptor antagonist widely used in the management of cardiovascular disorders such as hypertension, arrhythmias, and ischemic heart disease. By competitively inhibiting β-receptors, propranolol reduces heart rate, myocardial contractility, and overall cardiac workload, thereby counteracting the effects of endogenous and exogenous catecholamines like adrenaline [3,4].

Experimental evaluation of cardiac responses to pharmacological agents provides valuable insights into receptor-mediated mechanisms and drug interactions.

The administration of adrenaline typically produces a marked increase in heart rate and force of contraction, whereas propranolol attenuates or abolishes these effects through β-receptor blockade. Such studies are essential for understanding drug action, receptor sensitivity, and the physiological basis of therapeutic interventions targeting the cardiovascular system [5].Furthermore, the interaction between adrenergic agonists and antagonists serves as a classical model for studying competitive antagonism and receptor pharmacodynamics. Observing the extent to which propranolol inhibits adrenaline-induced cardiac responses helps in quantifying drug potency and efficacy, as well as elucidating receptor-specific mechanisms involved in cardiac regulation [6].Therefore, the present study aims to evaluate the cardiac responses induced by adrenaline and to assess the modulatory effects of propranolol in experimental models. This investigation contributes to a better understanding of β-adrenergic receptor function and

provides a pharmacological basis for the clinical use of β-blockers in cardiovascular diseases.

MATERIALS AND METHODOLOGY

Chemicals and reagents used

The materials used in this study included adrenaline (epinephrine) as the β-adrenergic agonist and propranolol as the non-selective β-adrenergic antagonist. Physiological salt solution such as Ringer's solution or Krebs-Henseleit solution was used to maintain the viability of the isolated heart preparation. Fresh experimental animal tissue (frog heart or isolated mammalian heart) was utilized for recording cardiac responses. Additional materials included distilled water, syringes for drug administration, and standard laboratory reagents required for maintaining physiological conditions during the experiment**.**

Instruments

The experiment was performed using an isolated heart setup equipped with a kymograph or digital data acquisition system for recording cardiac activity. A perfusion apparatus (Langendorff setup or simple organ bath system) was used to supply physiological solution to the heart. Supporting instruments included a force transducer for measuring contraction amplitude, a heart rate recording system, a thermometer to monitor temperature, and standard laboratory glassware such as beakers, pipettes, and measuring cylinders. All instruments were calibrated prior to the experiment to ensure accurate and reliable data recording**.**

Study Design

This study was conducted as a controlled experimental investigation to evaluate the pharmacodynamic effects of a β-adrenergic agonist (adrenaline) and a β-adrenergic antagonist (propranolol) on cardiac function. The design specifically aimed to characterize receptor-mediated responses and to determine the nature of drug interaction using dose-response analysis [7,8].

Experimental Model

An isolated heart preparation (frog heart in situ or Langendorff-perfused mammalian heart) was used to eliminate systemic influences such as neural reflexes and hormonal feedback. This model allows direct observation of cardiac responses to pharmacological agents under controlled conditions. The preparation was maintained at physiological temperature and continuously perfused with oxygenated physiological solution to preserve myocardial viability [9].

Reagents and Drug Preparation

Adrenaline and propranolol were freshly prepared in physiological saline before experimentation to ensure stability and activity. Serial dilutions of adrenaline (10^{-9} M to 10^{-5} M) were prepared to generate a graded dose-response curve. Propranolol was used at a fixed concentration (commonly 10^{-6} M) sufficient to produce measurable β-adrenergic blockade [10].

Tissue Preparation and Mounting

The experimental animal was handled according to standard ethical guidelines for laboratory use. The heart was carefully exposed and connected to the recording apparatus. In the Langendorff setup, the aorta was cannulated, and retrograde perfusion was initiated, whereas in frog heart preparations, drugs were applied directly to the cardiac tissue or sinus venosus. Care was taken to avoid mechanical damage to the myocardium during preparation [11].

Stabilization Phase

Following mounting, the heart was allowed to equilibrate for 10–15 minutes under continuous perfusion. During this period, spontaneous rhythmic contractions were monitored to ensure tissue viability and stability. Baseline parameters including heart rate and contraction amplitude were recorded.

Drug Administration Protocol

Adrenaline-Induced Responses

Adrenaline was administered in increasing concentrations in a cumulative or non-cumulative manner. After each dose, sufficient time was allowed for the response to reach a plateau. The following parameters were recorded:

- Increase in heart rate (positive chronotropy)
- Increase in force of contraction (positive inotropy)

These responses are mediated via β_1-adrenergic receptor activation, leading to increased intracellular cyclic AMP (cAMP) and enhanced calcium influx into cardiac muscle cells[12].

Washout Procedure

After completion of adrenaline dosing, the heart was perfused with fresh physiological solution to remove residual drug. This step ensured recovery to baseline conditions and prevented carryover effects.

Propranolol-Induced Blockade

Propranolol was administered at a predetermined concentration to achieve β-receptor blockade. The resulting decrease in heart rate and contractility was recorded. This effect occurs due to inhibition of cAMP formation and reduced calcium availability in myocardial cells.

Adrenaline in Presence of Propranolol

Adrenaline was re-administered following propranolol treatment. The responses were compared to those obtained prior to antagonist exposure. A diminished response indicated effective receptor blockade.

Dose-Response Curve Analysis

Dose-response curves were constructed by plotting log concentration of adrenaline against the percentage response. In the presence of propranolol, a rightward shift of the curve was observed. The EC_{50} (effective concentration producing 50% maximal response) was calculated for both control and antagonist conditions. The shift in EC_{50} without reduction in maximum response (Emax) confirmed the presence of competitive antagonism, indicating that propranolol reversibly competes with adrenaline for the same receptor binding sites[13].

Data Recording and Interpretation

All cardiac responses were recorded using a kymograph or digital acquisition system. The data were analysed for:

- Changes in baseline and drug-induced responses
- Magnitude of chronotropic and inotropic effects
- Reversibility of drug action

Statistical Analysis

Data were expressed as mean values (± standard deviation where applicable). Comparative analysis between control and treated groups was performed to assess the significance of observed differences [14].

Ethical Considerations

All experimental procedures involving animals were conducted in accordance with institutional ethical guidelines and standard laboratory practices to ensure humane handling and minimal distress.

RESULTS AND DISCUSSION

The present study clearly demonstrates the pharmacological effects of adrenaline and propranolol on cardiac function using an isolated heart model.

Adrenaline produced a dose-dependent increase in heart rate and contraction force, confirming its role as a β-adrenergic agonist. The observed positive chronotropic and inotropic effects are due to stimulation of β_1-receptors in cardiac tissue, leading to increased cyclic AMP (cAMP) production and enhanced calcium influx into myocardial cells. This results in stronger and faster cardiac contractions.

At higher concentrations, adrenaline caused marked tachycardia and increased contractility, indicating maximal receptor activation. The return of cardiac parameters to baseline following washout confirms that adrenaline's action is reversible and not permanently altering the tissue.

Propranolol, a non-selective β-adrenergic antagonist, produced a reduction in heart rate and contraction force, demonstrating effective β-receptor blockade. By competitively binding to β-receptors, propranolol inhibits the effects of endogenous or exogenous catecholamines, thereby reducing cardiac workload.

When adrenaline was administered in the presence of propranolol, the stimulatory effects were significantly reduced. This indicates that propranolol successfully blocks receptor sites, preventing adrenaline from exerting its full effect.

A key observation in this study is the rightward shift of the dose-response curve in the presence of propranolol. This shift, without reduction in maximum response, is a characteristic feature of competitive antagonism. It suggests that higher concentrations of adrenaline are required to overcome the inhibitory effect of propranolol, confirming that both drugs compete for the same receptor binding sites.

The reversibility of propranolol's effect further supports its competitive nature, as the blockade can be overcome either by increasing adrenaline concentration or by washing out the antagonist.

Clinically, these findings are significant. Propranolol is widely used in the management of cardiovascular conditions such as hypertension, angina, and arrhythmias. By reducing heart rate and myocardial oxygen demand, it provides protective effects against excessive sympathetic stimulation.

However, the study has limitations. The isolated heart model does not include systemic regulatory mechanisms such as autonomic reflexes and hormonal influences. Therefore, the responses observed may differ from those in a whole-body (in vivo) system.

Table 1: Effect of Adrenaline and Propranolol on Heart Rate and Contractile Force in Isolated Heart Preparation

Step	Experimental Phase	Drug / Condition	Concentration (M)	Heart Rate (BPM)	Contraction Force (g)	Observation
1	Baseline (Control)	Saline	—	60–72	2.5	Normal sinus rhythm
2	Adrenaline (Low Dose)	Adrenaline	10^{-8}	88	3.2	Initial stimulation
3	Adrenaline (High Dose)	Adrenaline	10^{-5}	145	5.8	Maximum tachycardia
4	Washout	Saline	—	74	2.6	Return to baseline
5	Propranolol	Propranolol	10^{-6}	64	2.1	β-blockade effect
6	Adrenaline + Propranolol	Prop + Adrenaline	10^{-5}	76	2.8	Inhibited response

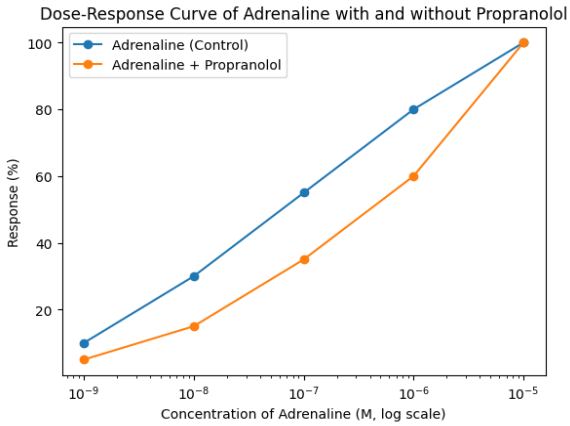

Figure 1: Dose–Response Curve of Adrenaline in the Absence and Presence of Propranolol

Clinical Correlation

The observed rightward shift in the dose-response curve is a classical indicator of competitive antagonism, which has significant clinical relevance. Propranolol, by competitively inhibiting β-adrenergic receptors, effectively reduces the effects of circulating catecholamines such as adrenaline. This mechanism plays a crucial role in the management of tachyarrhythmias, where excessive sympathetic stimulation leads to abnormally high heart rates. By blocking β-receptors, propranolol slows the heart rate and stabilizes cardiac rhythm, thereby preventing progression to severe arrhythmias. In addition, propranolol provides myocardial protection in conditions such as ischemic heart disease. By reducing the force of contraction (negative inotropic effect), it decreases myocardial oxygen demand, thereby minimizing the risk of ischemic damage during stress conditions.

Experimental Limitations

Although the present study provides valuable insights into cardiac pharmacology, certain limitations must be considered. Adrenaline is a non-selective agonist that acts on both α- and β-adrenergic receptors. However, in the isolated heart preparation, the observed effects are predominantly mediated through β_1-receptors due to the absence of vascular components. In an intact physiological system (in vivo), adrenaline also induces peripheral vasoconstriction via α-receptors, which can activate baroreceptor reflexes. This reflex may lead to a compensatory decrease in heart rate, a response that is not observed in isolated heart models. Therefore, the findings of this study may not fully represent the complex interactions occurring in a whole-body system.

Significance of Reversibility

An important observation in this study is the ability to overcome propranolol-induced blockade by increasing the concentration of adrenaline. This indicates that propranolol binds to β-adrenergic receptors through non-covalent and reversible interactions. The reversibility of this binding is a critical pharmacological feature, as it ensures that receptor function can be restored once the antagonist is removed or displaced. This property enhances the safety profile of propranolol, allowing the heart to respond to physiological demands when necessary. In contrast, irreversible receptor blockade would prevent normal sympathetic regulation, potentially leading to severe and life-threatening consequences. Therefore, the reversible nature of propranolol's action is essential for its therapeutic use in clinical practice.

CONCLUSION

The present study demonstrates that adrenaline significantly increases heart rate and contractile force through stimulation of β_1-adrenergic receptors, whereas propranolol effectively inhibits these effects by competitively blocking the same receptors. The observed rightward shift in the dose-response curve without reduction in maximum response confirms the presence of reversible competitive antagonism. These findings emphasise that cardiac activity is regulated by receptor-mediated mechanisms and can be modulated pharmacologically. The study also highlights the clinical importance of propranolol in reducing cardiac workload and managing conditions associated with excessive sympathetic stimulation. Overall, the interaction between adrenaline and propranolol provides a clear demonstration of fundamental pharmacological principles and their relevance in therapeutic applications.

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CONFLICT OF INTEREST

No

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