Aim: Study of Effect of Drugs on Isolated Heart

References:

1. Langendorff, O. (1895). Untersuchungen am überlebenden Säugetierherzen. Pflügers Archiv, 61(6), 291-332.

2. Curtis, M. J., & Walker, M. J. A. (1988). Quantification of arrhythmias using scoring systems: An examination of seven scores in an in vivo model of regional myocardial ischaemia. Cardiovascular Research, 22(9), 656-665.

3. Vogel, H. G. (2008). Drug Discovery and Evaluation: Pharmacological Assays. Springer.

Introduction:

The isolated heart preparation is a classical pharmacological method used to study the direct effects of drugs on heart function without the influence of systemic factors. This method allows for the precise control of experimental conditions and direct observation of drug actions on cardiac parameters such as heart rate, force of contraction, and rhythm.

Objective:

To study the effects of two different drugs (e.g., epinephrine and propranolol) on the isolated heart of a rat.

Materials and Reagents:

- Rat (200-250 g, either sex)
- Drugs: Epinephrine, Propranolol
- Krebs-Henseleit solution (KHS)
- Heparin (1000 IU/mL)
- Sodium pentobarbital (or other suitable anesthetic)
- Langendorff apparatus
- Perfusion pump
- Oxygen supply
- Water bath (37°C)

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- Pressure transducer and amplifier

- Data acquisition system

- Surgical instruments (scissors, forceps, hemostats)

- Syringes and needles

- Disposable gloves

- Laboratory coat

Preparation of Solutions:

- Krebs-Henseleit solution (KHS): Prepare freshly by dissolving the following in distilled water and aerate with 95% O2 and 5% CO2 to maintain pH 7.4:

- NaCl: 118 mM

- KCl: 4.7 mM

- CaCl2: 2.5 mM

- MgSO4: 1.2 mM

- NaHCO3: 25 mM

- KH2PO4: 1.2 mM

- Glucose: 11 mM

Procedure:

Animal Preparation

1. Anesthetize the rat with sodium pentobarbital (50 mg/kg, i.p.).

2. Administer heparin (1000 IU/kg, i.p.) to prevent blood clotting.

3. Once the rat is fully anesthetized, open the thoracic cavity to expose the heart.

Isolation of the Heart:

1. Rapidly excise the heart and immerse it in cold (4°C) KHS to arrest the heart.

2. Cannulate the aorta and connect it to the Langendorff apparatus to perfuse the heart retrogradely with oxygenated KHS at 37°C.

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Setting Up the Langendorff Apparatus:

1. Maintain a constant perfusion pressure (e.g., 70-80 mmHg) using a perfusion pump.

2. Attach a pressure transducer to measure heart rate and contractile force.

3. Allow the heart to stabilize for 20 minutes with continuous perfusion.

Baseline Recording:

1. Record the baseline heart rate, force of contraction, and rhythm using the data acquisition system.

2. Ensure that the baseline parameters are stable before administering any drugs.

Drug Administration and Recording:

Epinephrine

1. Prepare a stock solution of epinephrine and dilute it to the desired concentration with KHS.

2. Administer the epinephrine solution as a bolus into the perfusion line and observe the effects.

3. Record the heart rate, force of contraction, and rhythm for 10 minutes after administration.

Propranolol

1. Wash out the previous drug by perfusing with fresh KHS for 20 minutes or until baseline parameters are restored.

2. Prepare a stock solution of propranolol and dilute it to the desired concentration with KHS.

3. Administer the propranolol solution as a bolus into the perfusion line and observe the effects.

4. Record the heart rate, force of contraction, and rhythm for 10 minutes after administration.

Calculation and Analysis:

1. Calculate the percentage change in heart rate and force of contraction from baseline for each drug.

2. Compare the effects of the drugs on heart rate and force of contraction.

3. Analyze the data to determine the significance of differences between baseline and drug-treated conditions.

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Results and Discussion:

1. Present the data in tables and graphs showing heart rate and force of contraction before and after drug administration.

2. Calculate and present the mean percentage changes for each drug.

3. Discuss the results, explaining the pharmacological effects of each drug on the isolated heart.

- Epinephrine is expected to increase heart rate and force of contraction due to its action on β1-adrenergic receptors.

- Propranolol is expected to decrease heart rate and force of contraction due to its action as a β-adrenergic receptor antagonist.

Safety and Ethical Considerations

1. Ensure all experimental procedures involving animals comply with institutional and national ethical guidelines for the care and use of laboratory animals.

2. Handle all animals with care and minimize their distress.

3. Dispose of all biological waste according to safety guidelines.

Conclusion:

Summarize the findings, stating the observed effects of epinephrine and propranolol on the isolated heart and how these findings correlate with their known pharmacological actions.

Sample Data Table

Parameter	Baseline	Epinephrine (Mean ± SD)	% Change	Propranolol (Mean ± SD)	% Change
Heart Rate (beats/min)	300	400 ± 10	+33.3	250 ± 15	-16.7
Force of Contraction (g)	5	7 ± 0.5	+40.0	3 ± 0.4	-40.0

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