



Review Article

Screening/spot/colour test of anti-arrhythmic drugs

Ashok Kumar Jaiswal^{1,*}, Kamna Sharma², S Lukose³, Madhuri Gupta⁴

¹Dept. of Forensic Medicine and Toxicology, All India Institute of Medical Sciences, New Delhi, India

²Galgotias University, Greater Noida, Uttar Pradesh, India

³CTM-IRTE, Faridabad, Haryana, India

⁴Dept. of Pharmacology, All India Institute of Medical Sciences, New Delhi, India



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ABSTRACT

Anti-arrhythmic drugs are those drugs that are used to suppress abnormal rhythms of the heart. It acts as restoration of normal rhythms of the heart and conduction of the heart. These drugs directly or indirectly alter the membrane ion conductance, which in turn alters the physical characteristics of cardiac action potentials. In India, Forensic Science Laboratories run by Government under the Home ministry usually carry out this. The samples must be analyzed by the forensic toxicologist/chemists/scientist. This article deals with the screening/spot test for anti-arrhythmic drugs. An attempt has been made for screening/spot/colour test of anti-arrhythmic drugs in a stepwise manner, which can be of handy reference for the forensic toxicologist/scientist/chemist.

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1. Introduction

Anti-arrhythmic drugs that are used to treat abnormal heart rhythms due to irregular electrical activity of the heart. These disturbances can lead to alternations in overall cardiac functions that may be life-threatening. These drugs can be classified into four categories:¹⁻³

1. Class I Sodium channel blockers
2. Class II Beta Blockers
3. Class III Potassium channel blockers
4. Class IV Calcium channel blockers

1.1. Sodium channel blockers

These drugs bind and block the fast sodium channels that are responsible for the rapid depolarization. It reduces the velocity of action potential transmission within the heart. For example, quinidine, procainamide, etc.³

* Corresponding author.

E-mail address: ashokjaiswal72@gmail.com (A. K. Jaiswal).

1.2. Beta-blockers

These drugs reduce the blood pressure by blocking the effects of the hormone epinephrine. It causes the heart to beat more slowly and with the less force which in turn lowers the blood pressure. For example, Nadolol, propranolol, etc.³

1.3. Potassium channel blockers

These drugs act as inhibition of potassium efflux through the cell membrane. It is used to improve the motor function in patients with multiple sclerosis. For example, sotalol, amiodarone, etc.³

1.4. Calcium channel blockers

These drugs are used to lower blood pressure by slowing the activity of calcium into heart and blood vessels which in turn make it easier for the heart to pump. It also controls chest pain and irregular heartbeats. For example, Verapamil, etc.³

These approaches are designed to help the person think differently, change their expectations and behaviours. We have tried to set out standard procedures for screening/spot test for anti-arrhythmic drugs. which are easily available and useful for the forensic science laboratory. This article covers the spot test/colour test of Acebutolol, Ajmaline, Alprenolol, Amiodarone, Hydroquinidine, Lidocaine, Mexiletine, Nadolol, Oxprenolol, Prajmalium Bitartrate, Procainamide, Pindolol, Quinidine, Timolol and Verapamil.^{4–8}

2. Test of Anti-arrhythmic Drugs

2.1. Acebutolol

2.1.1. Nessler's test

1. Two to three drops of the extract are taken in a porcelain basin.
2. Two to three drops of Nessler's reagent is added to it.
3. The mixture is agitated & heated to 100°C in a water bath.
4. Orange colour is observed which indicates the presence of acebutolol.

2.1.2. Sulphuric acid test

1. Few drops of the extract are taken on a white tile or test tube.
2. Few drops of sulphuric acid are added to it.
3. The yellow colour is observed which indicates the presence of acebutolol.⁹

2.2. Ajmaline

2.2.1. Mandelin test

1. Two ml of extract is taken in a test tube.
2. Few drops of mandelin's reagent are added to it.
3. Red colour is observed which indicates the presence of ajmalin.¹⁰

2.2.2. Marquis test

1. Two ml of extract is taken in test tube.
2. Few drops of marquis reagent are added to it.
3. Violet colour is observed which indicates the presence of ajmaline.¹¹

2.2.3. Liebermann's test

1. Two ml of extract is taken in a test tube.
2. Few drops of Liebermann's reagent are added to it.
3. Red colour is observed which indicates the presence of ajmaline.

2.3. Alprenolol

2.3.1. Mandelin test

1. Two ml of extract is taken in a test tube.
2. Few drops of mandelin's reagent are added to it.

3. Play of colour from brown to violet is observed which indicates the presence of alprenolol.

2.3.2. Marquis test

1. Two ml of extract is taken in a test tube.
2. Few drops of marquis reagent are added to it.
3. Red colour is observed which indicates the presence of alprenolol.¹⁰

2.3.3. Liebermann's test

1. Two ml of extract is taken in a test tube.
2. Few drops of Liebermann's reagent are added to it.
3. Red colour is observed which indicates the presence of alprenolol.⁹

2.3.4. Sulphuric acid test

1. Few drops of the extract are taken on a white tile or test tube.
2. Few drops of sulphuric acid are added to it.
3. Orange colour is observed which indicates the presence of alprenolol.

2.4. Amiodarone

2.4.1. Sulphuric acid test

1. Few drops of the extract are taken on a white tile or test tube.
2. Few drops of sulphuric acid are added to it.
3. The yellow colour is observed which indicates the presence of amiodarone.

2.4.2. Liebermann's test

1. Two ml of extract is taken in a test tube.
2. Few drops of Liebermann's reagent are added to it.
3. Brown to yellow colour is observed which indicates the presence of alprenolol.

2.5. Hydroquinidine

2.5.1. Thalleioquin test

1. Few drops of the extract are taken on a filter paper.
2. One to two drop of thalleioquin reagent is added to it.
3. Green colour is observed which indicates the presence of hydroquinidine.¹¹

2.5.2. Sulphuric acid test

1. Few drops of the extract are taken on a white tile or test tube.
2. Few drops of sulphuric acid are added to it.
3. Yellow colour is observed which indicates the presence of hydroquinidine.

2.6. Lidocaine

2.6.1. Mercuric nitrate test

1. Two ml of extract in 2% solution of water is taken in a test tube.
2. Few drops of sulphuric acid are added to it.
3. 3 ml of mercuric nitrate solution are added to it.
4. The solution is heated to the boiling.
5. Yellow colour is observed which indicates the presence of lidocaine.

2.7. Mexiletine

2.7.1. Liebermann's test

1. Two ml of extract is taken in a test tube.
2. Few drops of Liebermann's reagent are added to it.
3. Brown colour is observed which indicates the presence of mexiletine.

2.7.2. Mandelin test

1. Two ml of extract is taken in a test tube.
2. Few drops of mandelin's reagent are added to it.
3. Brown to orange colour is observed which indicates the presence of mexiletine.

2.7.3. Marquis test

1. Two ml of extract is taken in a test tube.
2. Few drops of marquis reagent are added to it.
3. Red colour is observed which indicates the presence of mexiletine.¹²

2.8. Nadolol

2.8.1. Liebermann's test

1. Two ml of extract is taken in a test tube.
2. Few drops of Liebermann's reagent are added to it.
3. Brown colour is observed which indicates the presence of nadolol.

2.8.2. Marquis test

1. Two ml of extract is taken in a test tube.
2. Few drops of marquis reagent are added to it.
3. Red colour is observed which indicates the presence of nadolol.

2.8.3. Nessler's test

1. Two to three drops of the extract are taken in a porcelain basin.
2. Two to three drops of Nessler's reagent is added to it.
3. The mixture is agitated & heated to 100°C in a water bath.
4. Brown colour is observed which indicates the presence of nadolol.¹⁰

2.9. Oxprenolol

2.9.1. Marquis test

1. Two ml of extract is taken in a test tube.
2. Few drops of marquis reagent are added to it.
3. Violet colour is observed which indicates the presence of oxprenolol.

2.9.2. Mandelin test

1. Two ml of extract is taken in a test tube.
2. Few drops of mandelin's reagent are added to it.
3. Play of colour from grey to violet colour is observed which indicates the presence of oxprenolol.

2.9.3. Liebermann's test

1. Two ml of extract is taken in a test tube.
2. Few drops of Liebermann's reagent are added to it.
3. Black colour is observed which indicates the presence of oxprenolol.

2.9.4. Sulphuric acid test

1. Few drops of the extract are taken on a white tile or test tube.
2. Few drops of sulphuric acid are added to it.
3. Orange to red colour is observed which indicates the presence of oxprenolol.

2.10. Prajmalium Bitartrate

2.10.1. Mandelin test

1. Two ml of extract is taken in a test tube.
2. Few drops of mandelin's reagent are added to it.
3. Red colour is observed which indicates the presence of Prajmalium Bitartrate.

2.10.2. Liebermann's test

1. Two ml of extract is taken in a test tube.
2. Few drops of Liebermann's reagent are added to it.
3. Black colour is observed which indicates the presence of Prajmalium Bitartrate.⁹

2.11. Procainamide

2.11.1. Coniferyl alcohol test

1. Place a drop of extract of the sample is taken in a test tube.
2. A drop of coniferyl alcohol is added to it.
3. Filter paper is exposed to hydrochloric acid fumes.
4. Orange colour is observed which indicates the presence of procainamide.

2.11.2. Ninhydrin test

1. The residue is extracted in methanol.
2. One drop of extracted residue is taken on filter paper.
3. One drop of ninhydrin reagent is added to it.

4. Paper is air-dried in hot air.
5. Yellow colour is observed which indicates the presence of procainamide.¹⁰

2.12. Pindolol

2.12.1. Marquis test

1. Two ml of extract is taken in a test tube.
2. Few drops of marquis reagent are added to it.
3. Brown colour is observed which indicates the presence of pindolol.

2.12.2. Mandelin test

1. Two ml of extract is taken in a test tube.
2. Few drops of mandelin's reagent are added to it.
3. Green colour is observed which indicates the presence of pindolol.

2.12.3. Liebermann's test

1. Two ml of extract is taken in a test tube.
2. Few drops of Liebermann's reagent are added to it.
3. Blue to green colour is observed which indicates the presence of pindolol.

2.12.4. P-dimethylaminobenzaldehyde

1. Two ml of extract is taken in a test tube.
2. Few drops of p-dimethylaminobenzaldehyde reagent are added to it.
3. Red colour is observed which indicates the presence of pindolol.

2.13. Practolol

2.13.1. Liebermann's test

1. Two ml of extract is taken in a test tube.
2. Few drops of Liebermann's reagent are added to it..
3. Black colour is observed which indicates the presence of practolol.

2.14. Quinidine

2.14.1. Thalleioquin test

1. Few drops of the extract are taken on a filter paper.
2. One to two drops of thalleioquin reagent is added to it.
3. Green colour is observed which indicates the presence of quinidine.

2.14.2. Sulphuric acid test

1. Few drops of the extract are taken on a white tile or test tube.
2. Few drops of sulphuric acid are added to it.
3. Yellow colour is observed which indicates the presence of quinidine.

2.15. Sotalol

2.15.1. Liebermann's test

1. Two ml of extract is taken in a test tube.
2. Few drops of Liebermann's reagent are added to it.
3. Brown colour is observed which indicates the presence of sotalol.

2.15.2. Mercurous nitrate test

1. The extract is taken in powdered form in a test tube.
2. Few drops of Mercurous nitrate are added.
3. Few drops of ethanol are added to it.
4. Black colour is observed indicates the presence of sotalol.¹²

2.16. Timolol

2.16.1. Liebermann's test

1. Two ml of extract is taken in a test tube.
2. Few drops of Liebermann's reagent are added to it.
3. Violet colour is observed which indicates the presence of timolol.

2.17. Verapamil

2.17.1. Marquis test

1. Two ml of extract is taken in a test tube.
2. Few drops of marquis reagent are added to it.
3. Play of colour from yellow to green and finally to grey colour is observed which indicates the presence of Verapamil.⁹⁻¹²

3. Preparation of Solutions(9-12)

1. Coniferyl alcohol reagent: 0.1 g of coniferyl alcohol is warmed until it melt, dissolve in 3 ml of ethanol and diluted to 10 ml with water.
2. Liebermann's reagent: 1 gm of sodium or potassium nitrite is dissolved in 10 ml of sulphuric acid with cooling and swirling to absorb the brown fumes.
3. Mandelin's reagent: 1 g of ammonium vanadate is dissolved in 1.5 ml of water and dilute to 100 ml with concentrated sulphuric acid.
4. Marquis reagent: 100 ml of concentrated sulphuric acid is mixed with 1 ml of formaldehyde solution.
5. Nessler's reagent:
Reagent I : 50 g of mercuric chloride and 35 g of potassium iodide are dissolved in 200 ml of water.
Reagent II : 50 g of sodium hydroxide is dissolved in 250 ml of water.
Cold solution of Reagent II and Reagent I are mixed and made upto to 500 ml with water. Allowed the mixture to stand and decant the clear supernatant liquid for use. Store in dark brown bottles away from light.
6. Ninhydrin: 0.5 g of ninhydrin is dissolved in 40 ml of acetone.

7. p-Dimethyl amino benzaldehyde: 1 g of p-Dimethyl amino benzaldehyde is dissolved in 100 ml of ethanol. The solution is acidified with 10 ml of dilute hydrochloric acid.
8. Mercurous nitrate: 10 ml of a saturated solution of mercurous nitrate is added to 20 mg of Sodium bicarbonate.

4. Conclusion

In analysis of any poison, screening/spot test is especially useful for knowing the presence of the anti-arrhythmic drugs which can be confirmed by the more confirmatory tests. It saves time for the toxicologist, by helping them in ruling out the probability of poisons which can be confirmed by the more confirmatory tests and gives a quick clue to the doctors for patient management in emergency poisoning cases. The result of the analytical methods depends on the amount and purity of the sample extracted. Screening/spot test has been developed after repeated trial and testing. The techniques are being improved every time. It is important for the forensic toxicologists to know the best available method and help to detect the poison in criminal investigations.

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None.

6. Conflict of Interest

The authors declare that there is no conflict of interest.

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Author biography

Ashok Kumar Jaiswal, Chemist

Kamna Sharma, Research Scholar

S Lukose, Academic Head

Madhuri Gupta, Scientist

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