Review on: QUANTITATIVE ANALYSIS OF POTENT ANTIARRTHMATIC ACTIVE ENTITIES BY RP-HPLC.

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ABSTRACT
Analytical method development and its validation is a predominant feature in drug discovery process and Reverse Phase-High Performance Liquid Chromatography (RP-HPLC) is the most accepted analytical method utilized for analysis of drug due to its accuracy, selectivity and sensitivity. Development and validation of analytical method are providing accurate and precise data to ensure drug for its quality and safety. Sundry methods of analysis are reported/available for estimation of Anti-arrthmatic agent including RP-HPLC. This review article concisely discusses about analytical methods obtainable for the estimation of Anti-arrthmatic drugs substantially focusing on RP-HPLC.
KEYWORDS: - Anti-arrthmatic, Analytical method development, RP-HPLC.

INTRODUCTION

The technique of RP -HPLC is so called because of its improved performance when compared to other chromatographic techniques. Since high pressure is used when compared to other chromatography, it is so called as high pressure liquid chromatography. In reverse phase technique, stationary phase is a non-polar in nature and polar mobile phase is used. Hence, polar components get eluted first and non-polar compounds are retained for longer time. Due to the polar nature of the most of the drugs and pharmaceuticals, they are eluted faster and not retained for a longer time, which is advantageous. Different columns used are ODS (Octadecyl silane), C18, C8, C4, etc[1] .Table 1 represents the classification of Anti-arrthmatic drugs based on their chemical structure[2].

Table 1
Chemical classification of Anti-arrthmatic agents[2].

Class	Action	Drugs
1.	Membrane stabilizing agents(Na^+ channel blockers)	
	A. Moderately decrease dv/dt of 0 phase	Quinidine, Procainamide, Disopyramide
	B. Little decrease in dv/dt of 0 phase	Lidocaine, Mexiletine
	C. Marked decrease in dv/dt of 0 phase	Propafenone, Flecainide
2.	Antiadrenergic agents	Propranolol, Esmolol,Sotalol
3.	Agents widening AP	Amiodarone, Bretylium, Dofetilide , Ibutilidine
4.	Calcium channel blocker	Verapamil, Diltiazem
IN Addition		
5.	For PSTV	Adenosine, Digitalis
6.	For A-V block	Symathomimetics-Isoprenaline Anticholinergics-Atropine
7.	Digitalis in used in AF,AFI, and PSTV to control ventricular rate	

Table 2

Chromatographic condition for Anti-arrthmatic class 1 drugs: membrane stabilizing agent(Na^+ channel blocker) A: Moderately decrease dv/dt of 0 phase

Name of Drug	Sample Matrix	Chromatographic Condition	Mobile Phase	Detection
Quinidine[3]	Bulk and tablet dosage form	Phenomenex C-8, (250mm x 4.6mm, 5 µm)	Methanol:sodium dihydrogen ortho phoshphate buffer(70:30v/v)	UV Detection At 250nm
Quinidine[4]	Bulk and capsule dosage form	ODS C18 (250mm X 4.6 mm i.d., 5 µm particle size)	Phosphate buffer (pH 4.5): Methanol (55: 45 v/v)	UV detection at 234 nm
Quinidine[5]	Pharmaceutical dosage form	C-4 column,(250 mm x 4.6mm, 5 µm)	ammonium acetate buffer (0.02 M, pH 3.5) and acetonitrile (30:70 v/v)	UV Detection At 250nm
Procainamide[6]	Plasma	10cmx4 mm Novapak reversedphase (5 pm) equipped with a 2 cm guard column for RP column (37 to 53 P>	Water:methanol:acetic acid:triethylamine (74:25:1:0.03 v/v/v/v)	UV detection at 280 nm
Procainamide[6]	Plasma and drugs	25 cm x 4.6 mm of ultrasphere ODS (5 pm) with a guard column (3 cm x 4 mm) of pBondapak C18 - Corasil (37-50 pm)	0.05M KH_2P0_4 (pH 2.5) - acetonitrile	220 nm to 280 nm
Procainamide[6]	Bulk and Pharmaceutical dosage form	12.5 cm x 4.9 mm of Sherisorb s5w	Methanolic 10 mM Ammonium perchlorate and methanolic 0.1 M-sodium hydroxide (pH 6)	UV detection at 254 nm
Procainamide[6]	Human serum	15 cm x 3.9 mm of Novapak clg FLm)	Acetic acid;water:acetonitrile (2:50:5v/v/v) containing 3.5% of sodium acetate	UV detection at 254 nm
Procainamide[6]	Serum and plasma	10cmx5 mm of Novapak cyano HP.	5mM acetate buffer (pH 6) containing 0.05% triethylamine and 10% acetonitrile	UV detection at 280nm
Procainamide[6]	Bulk and Pharmaceutical dosage form	10 cm x 4.6 mm Brownlee RP-8 (5 pm)	100% methanol:aqueous phosphate buffer (pH 3) (1:l v/v)	UV detection at 460nm
Procainamide[6]	Bulk and Pharmaceutical dosage form	5cmx4 mm of Nucleosil 5SA (5 pm)	0.1 Mphosphate buffer (pH 3) containing 30% of acetonitrile.	UV detection at 280 nm
Procainamide[6]	Serumand urine	15 cm x 4.5 mL IBM phenyl(5 elm.).	75 mM Acetate buffer(pH4.3) acetonitrile (20:3 v/v)	UV detection at 270nm
Procainamide[6]	Human blood plasma	15 cm x 4.8 mm stainless steel, packed with Nucleosil CIS (5 pm.1.	Methanol : acetic acid : triethylamine : water (40:2:1:157 v/v/v/v)	UV detection at 335 nm(extraction at 290 nm)
Procainamide[6]	Serum	25 cm x 4.6 mm of CNtype (5um) material operated at 40’ c	Acetonitrile:methanol : buffer (60: 7 : 3 v/v/v), buffer is 10 mM phosphate - 0.5 mMtriethylamine, pH was adjusted to 7.1	UV detection at 205 nm
Procainamide[6]	Human serum	pBondapak ODS	Aqueous 35% methanol : 0.06M acetate buffer (pH 4.5).	UV detection at 220 nm
Procainamide[6]	Serum	CS Reversed phase column.	80% Phosphate buffer (25 mmol/L, pH3.4)20% organic (acetonitrile: methanol, 2:3 v/v) and then changed to 30% phosphate 70% organic at 20 min after inject ion.	UV detection at 212 nm
Procainamide[6]	Biological fluid	30 cm x 4 mm i.d.	Acetonitrile phosphate buffer	UV detection at

		of alkylphenyl column	pH 6.6 column (60:40 v/v)	280 nm
Procainamide[6]	Serum	15 cm x 4.6 mm i.d. of S ynchropak SCD-100 (5 Pm)	25 mM- Ammonium sulfate (pH 7.3) containing 24% of acetonitrile	UV detection at 230 nm
Procainamide[6]	Serum	0.5 m x 2.6 mm i.d. of ODS-SIL-X	Acetonitrile: phosphate buffer (1 0:90 v/v).	UV detection at 205 nm
Disopyramide[7]	Human plasma	5-µm Supelcosil CN 25 cm X 4.6 mm column	Gradient: Mobile phase I, acetonitrile25 mM :sodium phosphate, pH 6.8 (50:50v/v) Mobile phase II, acetonitrile-25 mM :sodium phosphate, pH 6.8 (38:62v/v)	UV Detection At: 215nm
Disopyramide[8]	Pharmaceutical dosage form	10-µm Lichrosorb RP-18 250 mm X 4 mm column	Acetonitrile : methanol:phoshphate buffer(PH 3.2)(6:1:3,v/v/v)	UV Detection At: 269nm

Table 3

Chromatographic condition for Anti-arrthmatic class 1 drugs: membrane stabilizing agent(Na^+ channel blocker) B: Little decrease in dv/dt of 0 phase

Name of Drug	**Sample Matrix**	**Chromatographic Condition**	**Mobile Phase**	**Detection**
Lidocaine[9]	Topical formulation	HiQSilHSC18column (250 mm × 4.6 mm, 5 µm).	acetonitrile: 0.01 M diethylamine solution (pH adjusts to 6.8 with orthophosphoric acid) (60:40 v/v)	UV Detection At: 225nm
Lidocaine[10]	Human serum	Alltima C18-column (150 × 4.6 mm) i.d., 3.5 µm	acetonitrile and phosphate solution (25 mM KH2PO4-3 mM sulfuric acid-3.6 mM triethylamine) in a ratio of 12:88 (v/v)	UV Detection At: 210nm
Lidocaine[11]	Pharmaceutical dosage form	ODS 4.6 mm x15 cm, 5 µm	Water and acetonitrile(72:28v/v) pH adjusted to 2.0 with 85% orthophoshphoric acid	UV Detection At: 208nm
Lidocaine[12]	Mouthwash formulauion	Waters Symmetry C18 HPLC column (150 mm × 4.6 mm, 5 µm)	methanol - 0.1M Sodium dihydrogen phoshphate with a pH that was previously adjusted to 4.5 with dilute phosphoric acid with gradient elution.	UV Detection At: 230nm
Lidocaine[13]	Pharmaceutical dosage form	C18 Hypersil BDS column	Briton-Robinson buffer, pH 7: methanol:acetonitrile (40: 45: 15 v/v/v)	UV Detection At: 225nm
Lidocaine[14]	Pharmaceutical gel	5 mm LichroCART RP-18 column (125 mm x 4 mm i.d.)	acetonitrile: 0.05 M sodium phosphate buffer, pH 6.0 (35:65 v/v) and 0.05% of diethylamine	UV Detection At: 210nm
Lidocaine[15]	Tablet and Injection	Spherisorb ODS (5 microm) (4.6 mm x 250 mm(2))	5.5% triethylamine in acetonitrile/water(70/30 v/v)	UV Detection At: 254nm
Mexiletine[16]	Capsule	5 µm LiChrospher 60, RP-Select B column (250mm ×4 mm ID)	1.28 g dodecyl sodium sulfate and 4.00 g of anhydrous sodium dihydrogen phosphate in 600 mL of water (pH 4.5) acetonitrile (60 : 42, v/v).	UV detection at 262 nm

Table 4

Chromatographic condition for Anti-arrthmatic class 1 drugs: membrane stabilizing agent(Na^+ channel blocker) C: Marked decrease in dv/dt of 0 phase

Name of Drug	Sample Matrix	Chromatographic Condition	Mobile Phase	Detection
Propafenone[17]	Blood sample	Spherisorb SCN column(4.6 mm x 120mm)3 µm	Acetonitrile:buffer(7.7 gm ammonium acetate 900 ml water then it is acidified with acetic acid pH 6.0 that it will diluted till 1000 ml.(50/50 v/v)	UV detection at 248 nm
Propafenone[18]	Tablet	Inerstil ODS-3 Vs column	Gradient; Solvent A: Acetonitrile(75) Solvent B : methanol:water(90:10)	UV detection at 245 nm
Flecainide[19]	Bulk powder and dosage form.	RP-C18 column	phosphate buffer pH 3.3:acetonitrile:triethylamine (53:47:0.03v/v/v)	UV detection at 292 nm
Flecainide[20]	Biological specimen	HYPERSIL BDS Phenyl column (53mm X 7.0 mm),3 µm	Gradient: Solvent A: Water:Methanol:1.5 M ammonium acetate (87:10:3 V/V/V) Solvent B: Water:Methanol:1.5 M ammonium acetate (17:80:3 V/V/V)	UV detection at 230nm

Table 5

Chromatographic condition for Anti-arrthmatic class 2 drugs: Antiadrenergic agents

Name of Drug	Sample Matrix	Chromatographic Condition	Mobile Phase	Detection
Propanolol[21]	Tablet	XTerra RP18(150mm X 4.6 mm,5 µm)	Pyrrolidine(pH 11.5):acetonitrile(50:50 v/v)	UV detection at 214 nm
Propranolol[22]	Bulk and pharmaceutical dosage form	Thermo-hypersil c8 column (250mm x 4.6 mm,5 µm)	Acetonitrile: 0.01 M ammonium phosphate buffer (pH:3 adjusted by orthophoshphoric acid) (50:50 v/v)	UV detection at 238nm
Propranol[23]	Pharmaceutical dosage form	C18 column(Inersil c18,250mm x 4.6 mm, 5 µm)	Methanol:acetonitrile:water(50:30:20 v/v/v)	UV detection at 232 nm
Propranolol[24]	Tablet dosage form	Agilent C18 (250 4.6 mm, 5 µm)	0.02 M sodium Phoshphate buffer: acetonitrile(65:35 v/v)	UV detection at 240 nm
Propranolol[25]	Bulk and pharmaceutical dosage form	Agilent xdb C18(150 mm X 4.6 mm, 5 µm)	Methanol:acetonitrile:potassium dihydrogen phoshphate(adjusted pH 3.0 using orthophoshphoric acid),(20:20:60,v/v/v)	UV detection at 264 nm
Esmolol[26]	Bulk and pharmaceutical dosage form	C 18 column(250mm x 4.6 mm, 5 µm)	Acetonitrile:0.05 M sodium acetate buffer : glacial acetic acid(35:65:3 v/v/v)	UV detection at 275 nm
Sotalol[27]	Tablet	C 18 column(100mm x 4.6 mm, 5 µm)	Methanol:Acetonitrile: 20 mM ammonium acetate (pH-6)(15:10:75 v/v/v)	UV detection at 229 nm
Sotalol[28]	Oral liquid	Ascentic express c18(100 mm x4.6 mm, 2.7 µm)	Gradient phase :sodium dihydrogen phoshphate dehydrate: acetonitrile	UV detection at 237 nm

Table 6
Chromatographic condition for Anti-arrthmatic class 3 drugs: Agents widening AP

Name of Drug	Sample Matrix	Chromatographic Condition	Mobile Phase	Detection
Amiodarone[29]	Bulk and pharmaceutical dosage form	Hypersil BDS C 18 column(100mm x 4.6 mm, 5 µm)	0.5% v/v TEA buffer pH 6.5 and acetonitrile (25:75 v/v)	UV detection at 240 nm
Amidarone[30]	Bulk and pharmaceutical dosage form	Hi Q SIL C 18(4.6mm x 520 mm, 5 µm)	Acetonitrile:0.5% formic acid(80:20 v/v)	UV detection at 242 nm
Amiodarone[31]	Tablet	C 18 column(150mm x 4.6 mm, 5 µm)	Buffer solution pH 5.0(prepared by 3.0ml acetic acid in 1000 ml water and adjusted pH 5.0 with dilute ammonia solution):methanol:acetonitrile(30:30:40 v/v/v)	UV detection at 240nm
Bretylium[32]	Pharmaceutical dosage forms	Inersil ods 2(150mm x 4.6 mm,5 µm)	Gradient: Eluent A: 1 ml TFA in 1000 ml water Eluent B: 1 ml TFA in 1000ml aetonitrile	UV detection at 215 nm
Bretylium[33]	Pharmaceutical dosage forms	XBridge C-18 Column(150mm x 4.6mm,5 µm)	3 mol KOH buffer solution ph 10.50:methanol(60:40v/v)	UV detection at 215 nm
Dofetilide[34]	Plasma	Ultrasphere ods c18 (250x4.6mm,5 µm)	Gradient: Buffer A:methanol/ammonium phoshphate , 1-heptane-sufonate:acetonitrile(19:70:11 v/v/v) containing 0.08% triethylamine and adjusted pH7.1 with phoshphoric acid Buffer B:methanol/ammonium phoshphate, 1-heptane-sulfonate:acetonitrile(38:4:20 v/v/v) containing 0.08% triethylamine and adjusted pH7.1 phoshphoric acid	UV detection at 238nm
Dofetilide[35]	Bulk and pharmaceutical dosage form	Phenomenex c18 (150x4.6 mm,1.8 µm)	Potassium dihydrogen phoshphate buffer pH 6.8:acetonitrile:methanol(50:30:20 v/v/v)	UV detection at 231 nm
Ibutilide[36]	Pharmaceutical manufacturing eniornment	Inersil c8 250x 4.6 mm,5 µm	Gradient phase Solvent A:0.01 M potassium dihydrogen phoshphate Solvent B:acetonitrile	UV detection at 227 nm
Ibutilide[37]	Bulk and pharmaceutical dosage form	Hypersil c18 (250x4.6 mm,5 µm)	Acetonitrile:0.1 M ammonium dihydrogen phosphate buffer pH-6.0 (25:75 v/v)	UV detection at 250 nm
Ibutilide[38]	Pharmaceutical dosage form	Hypersil c18 (250x4.6 mm,5 µm)	Methanol:water(55:45 v/v)	UV detection at 228 nm
Ibutilide[39]	Injection	Vp-ODS column(250mm x 4.6 mm,5 µm)	0.06 M l-1 potassium dihydrogen phoshphate pH 5.8:methanol:triethylamine(45:55:0.01v/v/v)	UV detection at 228 nm

Table 7
Chromatographic condition for Anti-arrthmatic class 4 drugs : Calcium channel blocker

Name of Drug	Sample Matrix	Chromatographic Condition	Mobile Phase	Detection
Verapamil[38]	Pharmaceutical dosage form	Hypersil c18 (250x4.6 mm,5 µm)	Methanol:water(55:45 v/v)	UV detection at 228 nm
Verapamil[40]	Human plasma	Lichrosphere 60 RP- select Bcolumn(250 mm x 4mm,5 µm)	Acetonitrile:0.025 mol/l potassium dihydrogen phosphate (40:60 v/v)	UV detection at 200 nm
Verapamil[41]	Human plasma	Cyanopropylsilane column	Acetonitrile:0.02 M acetate buffer pH 7.0(65:35 v/v)	UV detection at 228 nm
Verapamil[42]	Capsule	Lichrosorb RP18 column	Acetonitrile:methanol:phosphate buffer pH 2.7(40:40:20 v/v/v)	UV detection at 220 nm
Verapamil[43]	Pharmaceutical dosage form	C18 reverse phase column	Methanol:water:acetic acid:triethylamine(55:44:1:0.1v/v/v/v)	UV detection at 280nm
Verapamil[44]	Plasma	C18 reverse phase	Gradient:	Fluorescence

		column	Mobile phase A: 50 mM ammonium phoshphate,pH 4.5) Mobile phase B: 50mM ammonium phosphate:acetonitrile(70:30 v/v)	detector excitation 313 nm and emission 280nm
Verapamil[45]	Residue	Hypersil ODS (125 x 4.0 mm,5 µm)	Methanol:water:triethylamine(70:30:0.2 v/v/v)	UV detection at 278 nm
Diltiazem[46]	Tablet	Hypersil bds c18(150 mmx 4.6 mm,5.0 µm)	Gradient : Mobile phase A:0.2%triethylamine pH adjusted to 4.5 with orthophosphoric acid Mobile phase B:acetonitrile	UV detection at 240 nm
Diltiazem[47]	Raw and pharmaceutical forulation	Hypersil ODS C 18(150mm x4.6 mm,5 µm)	Methanol:water(80:20 v/v)	UV detection at 236 nm
Diltiazem[48]	Plasma	Spherisorb c18	Methanol:water containing 2.8 mM triethylamine(80:20 v/v)	UV detection at 239 nm
Diltiazem[49]	Drug metal interaction	Shim pack CLC – ODS(6.0mm x150 mm)	Acetonitrile:water(40:60 v/v),pH adjustedto 2.8 with phoshphoric acid	UV detection at 235 nm
Diltiazem[50]	Plasma	Zorbax SB c18(250mm x4.6 mm,5 µm)	0.2 m ammonium dihydrogen phoshphate :acetonitrile:isopropyl alcohol:triethylamine(55:43:1.7:0.3 v/v/v/v)	UV detection at 240 nm
Diltiazem[51]	Raw and pharmaceutical dosage form	Rp c-18(250mm x 4.6 mm,5 µm)	0.01 M ammonium acetate in water:methanol:acetonitrile(700:240:60 v/v/v)	UV detection at 295 nm
Diltiazem[52]	Pharmaceutical and human serum	Hiber rp c-18(250mm x 4.6 ,5 µm)	Acetonitrile:water(85:15 v/v)	UV detection at 230 nm
Diltiazem[53]	Raw material	Microbonapack c 18 column(250mm x 4.6 mm, 5 µm)	0.1 M sodium acetate buffer pH 6.3:acetonitrile(65:35 v/v)	UV detection at 240 nm
Diltiazem[54]	Plasma	Agilent TC c18 column(250mm x 4.6 mm, 5 µm)	Methanol:water(90:10 v/v)	UV detection at 237 nm

Table 8
Chromatographic condition for Anti-arrthmatic class 5 drugs : For PSTV

Name of Drug	Sample Matrix	Chromatographic Condition	Mobile Phase	Detection
Adenosine[55]	Kinase	C 18 column	Water:acetonitrile(93:7 v/v)	UV detection at 260 nm
Adenosine[56]	Intracellular	Luna c18(250mm x 4.6 mm, 5 µm)	Acetonitrile:50 mM monobasic potassium phosphate pH 4.6(0.5:99.5 v/v)	UV detection at 254 nm
Adenosine[57]	Human synovial fluid	ODS (250mm X 4.6 mm,5 µm)	Phoshphate buffer and acetonitrile(90:10 v/v)	UV detection at 260 nm
Digitalis[58]	Leaves	Octylsilyl bonded silica column	Acetonitrile:methanol:water(10:15:18 v/v/v)	UV detection at 220 nm
Digitalis[59]	Tablet (digoxin)	Symmetry c 18 (75mm x 4.6 mm, 3.5 µm)	Water:acetonitrile(72:28 v/v)	UV detection at 220nm

Table 9
Chromatographic condition for Anti-arrthmatic class 6 drugs:For A-V block A:Symathomimetics

Name of Drug	Sample Matrix	Chromatographic Condition	Mobile Phase	Detection
Isoprenaline[60]	Injection	Eclipse XDB C-18(250mm x 4.6 mm,5 µm)	0.14% sodium heptan esulfonate with adjusted pH 3.5 with orthophosphoric acid:methanol (65:35v/v)	UV detection at 280 nm

Table 10
Chromatographic condition for Anti-arrthmatic class 6 drugs: For A-V block B:Anticholinergics

Name of Drug	Sample Matrix	Chromatographic Condition	Mobile Phase	Detection
Atropine[61]	Ophthalmic formulation	ODS –BP hyperchrome c 18 column(250mm x 4.6 mm,5 µm)	0.05 M potassium dihydrogen phosphate buffer pH 4.0:acetonitrile(60:40 v/v)	UV detection at 266 nm
Atropine[62]	Raw Material	C 18 column	Methanol :5 mM potassium dihydrogen phosphate buffer(50:50v/v)	UV detection at 264 nm
Atropine[63]	Eye drops	c-8 column	Acetonitrile:dilute acetic acid (80:20 v/v)	UV detection at 260nm

Conclusion

This review briefs about the analytical methods development and validation of anti-arrthmatic drugs in various pharmaceutical formulations, bulk and biological samples alone or in combination with other drugs by using RP-HPLC.
Purpose of using RP-HPLC method is for estimation of anti-arrthmatic drugs and validated that method as per ICH guideline. Beneficial properties of RP-HPLC method for estimation of anti-arrthmatic drugs is its high sensitivity, accuracy and reproducibility.
Also the article will be very beneficial for many researchers working in the area of estimation of anti-arrthmatic drugs as they can refer most of the RP-HPLC methods of estimation of anti-arrthmatic drugs by referring this single article.

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