A Review on Analytical Methods for Ranolazine determination in synthetic mixture

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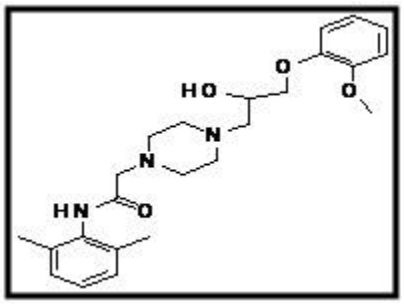
ABSTRACT

Ranolazine is a piperazine derivative is a new anti-ischemic drug for the treatment of angina.
Ranolazine is to inhibit late INa thus preventing sodium overload of the cell. As a consequence, ranolazine prevents reverse mode sodium-calcium exchange and thus diastolic accumulation of calcium possibly resulting in improved diastolic tone and improved coronary blood flow.
This review article represent the various analytical methods which has been reported for estimation of Ranolazine in synthetic mixture. The spectrophotometric techniques like fluorescent assay and area under curve spectroscopy ; Chromatogrraphic methods like HPLC, HPTLC and RP HPLC, GC, LC-MS, LC-MS/MS were reported.

Keywords: Ranolazine, anti-ischemic, Angina

INTRODUCTION[1]

Ranolazine is -(2,6-dimethylphenyl)-2{4-[2-hydroxy-3-(2-methoxyphenoxy)propyl piprazine-1-yl} aceta -mide is piprazine derivative appears as white to off white crystalline powder. The drug is freely soluble in Methanol. Ranolazine is a strong base with pKa values of 13.6, Six-membered Piprazine Ring. Ranolazine melts at 122-124 ^{0}C.



Chemical formula: $C_{24}H_{33}N_3O_4$
Molecular weight: 427.54 g/mol

Figure:1 Structure of Ranolazine

MECHANISM OF ACTION[2]

Ranolazine a piperazine derivative is a new anti-ischemic drug for the treatment of angina. Ranolazine is to inhibit late I_{Na} thus preventing sodium overload of the cell. As a consequence, ranolazine prevents reverse mode sodium-calcium exchange and thus diastolic accumulation of calcium possibly resulting in improved diastolic tone and improved coronary blood flow.

As a late I_{Na} inhibitor, ranolazine was also shown to increase action potential duration and thus modestly QT interval by 2-5 ms. This effect, however, is not heart rate-dependent and cannot be exaggerated during bradycardia. Furthermore, ranolazine does not induce early after depolarization and does not increase dispersion of repolarization across the left ventricular wall.[2]

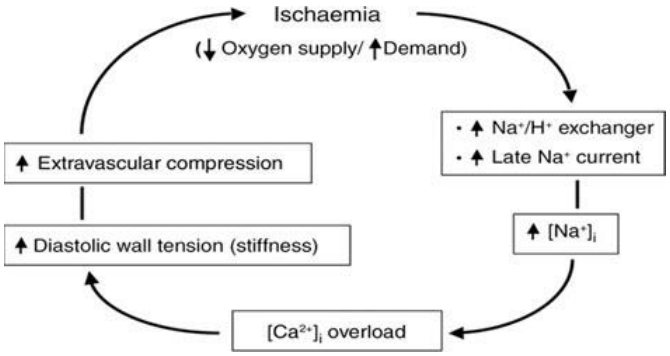


Figure 2:Mechanism of Ischaemia

It is act via selective inhibition of the late inward sodium current (I_{Na}) in cardiac muscle cells. This reduces intracellular sodium accumulation and calcium overload, and consequently improves myocardial relaxation and decreases left ventricular diastolic stiffness.

Ranolazine is administered orally and metabolize by CYP3A and excreted in intestine (5%) and in urine

Analytical Method

A. Compendial Method:

Ranolazine is not official in Pharmacopoeia.

B. Reported Method:

I. Chromatographic Methods

The high-pressure liquid chromatography (HPLC) for Ranolazine estimation. GC method for residual solvent determination in Ranolazine. HPTLC method are widely used chromatographic methods in the analysis of Ranolazine in Formulation. LC-MS/MS, LC-MS and UHPLC use for estimation of Ranolazine in Plasma. RP HPLC method also developed for determination of concentration of Ranolazine in human serum and also for simultaneous determination of Ranolazine and Dronederone.

Table No.1: Summary of Chromatographic Method of Ranolazine

Title	Method	Mobile phase	Stationary phase	Wave Length	REF.
Ranolazine in bulk & marketed formulation	HPLC & UV	Methanol : 0.5% tri ethyl amine pH 6 with orthophosphoric acid (75:25)	-	271	3
Estimation of Ranolazine HCL in Tablet Dosage Form	RP-HPLC	Buffer : Acetonitrile(60:40),(pH adjust with triethylamine	Inertsil ODS C18	224 nm	4
Determination of Ranolazine HCL in bulk and dosage form	LC	Methanol : water (99:1 %,V/V)	HiQ Sil C_{18} HS	273 nm	5
Quantitation of Ranolazine in rat plasma	LC	Acetonitrile : water : formic acid : 10% *n*-butylamine (70:30:0.5:0.08, v/v/v/v)	Nova-Pak C_{18} column	-	6
Determination of Ranolazine in human plasma	HPLC	Acetonitrile: 0.1% formic acid(90:10)	Agilent-ZORBAX C_{18} column	-	7
Estimation of Ranolazine in Human Plasma	LC	methanol-10mM ammonium acetate (60:40 v/v, pH 4.0)	Zorbax extend C_{18} column	-	8
Ranolazine HCL in bulk and tablet dosage form	HPTLC	Chloroform: methanol : toluene (5 : 1 : 1 v/v/v)	silica gel aluminium plate 60 F - 254	273 nm	9
Determination of residual solvents in Ranolazine	GC	-	HP-INNOWAX column	-	10

II. UV spectroscopic method

First order derivative spectroscopy and Area Under curve spectroscopic technique was developed for simultaneous determination of Ranolazine was developed.

Table No.2: Summary of UV spectroscopic method

Title	Method	Wavelength	Linearity and R^2	Recovery	REF.
Estimation of Ranolazine in bulk drug and pharmaceutical formulation	UV method	272 nm	10-100 µg/ml	99.77-100.33 %	11

Estimation of Ranolazine in bulk and pharmaceutical dosage form	First order derivative spectroscopic method	263 nm and 282 nm	10-35 µg/ml and 0.9992	-	12
Estimation of Ranolazine in API and tablet formulation	Area under curve method	261nm and 281 nm	75-200 µg/ml and 0.998	99.42-99.97 %	13

Table No.3: HPLC Method for simultaneous estimation of Ranolazine and Dronederone

Title	Method	Mobile phase	Stationary phase	Wave length	REF.
Simultaneous estimation of Ranolazine and Dronederone in bulk and pharmaceutical dosage forms.	HPLC	0.02N NH_2PO_4 buffer (pH 4) : Acetonitrile (50 :50 V/V)	ODS column	282 nm	14

DISCUSSION

Presented systematic review covers the current analytical methods for the determination of Ranolazine and its combination in pharmaceutical and biological samples like serum and plasma. HPLC method were found to be most widely use for Ranolazine. Various chromatographic conditions are presented in table.

CONCLUSION

The sensitivity, specificity, and better separation efficiency enable HPLC to be used frequently for simultaneous qualitative and quantitative determination of Ranolazine. The presented information is useful for the future study for researcher involved in formulation development and quality control of Ranolazine.

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