2. REVIEW OF LITERATURE

There are many methods available for the analysis of cardiovascular drugs. Those include both classical and instrumental methods. The methods have been developed keeping in view the requirements. Consequently, certain methods are also focused on the analysis of the drug from biological fluids.

Whatever methods given in tables is developed on single drug formulations and on combination drug formulations but there are many new combinations available of following drugs on which the work has not been done and it is not published yet, so our aim is to select such combination formulations for developing method.

2.1.1 Official Methods for Amlodipine

**Indian Pharmacopoeia, (2010)**\(^9\), describes the method for estimation of amlodipine besilate in tablet dosage form where S.P: Octadecylsilane silica gel (5 \( \mu \)m) (150 mm x 3.9 mm i.d.) M.P: Buffer solution (7 ml of Triethylamine in 1 litre of water and adjust pH 3.0 ± 0.1 with phosphoric acid): methanol: Acetonitrile (50:35:15) Flow rate: 1 ml/min, Detection: 237nm, Injection volume: 10 \( \mu \)l was utilized.

**British Pharmacopoeia, (2009)**\(^10\), describes the method for estimation of amlodipine besilate in tablet dosage form where S.P: Octadecylsilyl silica gel (5 \( \mu \)m) (150 mm x 3.9 mm i.d.), M.P: 15 ml Acetonitrile: 35 ml Methanol: 50ml Buffer solution (7 ml of Triethylamine in 1 litre of water and adjust pH 3.0 ± 0.1 with phosphoric acid), Flow rate: 1 ml/ min, Detection: 237 nm, Injection volume: 10 \( \mu \)l was utilized.

**Japanese Pharmacopoeia, (2011)**\(^11\) describes the method for estimation of amlodipine besilate in tablet dosage form where S.P: Octadecylsilyl silica gel (5 \( \mu \)m) (4.6 mm i.d x 150 mm length), M.P: A mixture of methanol and potassium dihydrogen phosphate (41 in 10,000) (13:7), Flow rate: 1 ml/ min, Detection: 237 nm, Injection volume: 20 \( \mu \)l was used.

2.1.2 Reported methods of Amlodipine besilate

**Jaina N, et al. (2010)**\(^12\) developed method for estimation of Amlodipine besilate in bulk drug and Tablet dosage form where solvent used is Sodium Acetate for the range of 50-250 ug/ml of Amlodipin and detected the absorbance at 365 nm.\(^12\)
Mehulkumar P, et al. (2009)\textsuperscript{13} Developed method for Simultaneous Spectroscopic Estimation of Amlodipine Besylate and Olmesartan Medoximil by derivative spectroscopic method in Tablet Dosage Form where ZCP: 239 nm of AMLO and 255 nm of OLME, Solvent: Methanol: water (1:4), Range: 2.5-30 μg/ml of AMLO and 4-32 μg/ml of OLME was taken as a method parameter.

Prasad C.V, et al. (2011)\textsuperscript{14} developed method for Simultaneous Spectroscopic Estimation of Amlodipine Besylate and Hydrochlorothiazide in Tablet dosage form using simultaneous equation method where both drugs detected at 238 nm and 271 nm respective using Solvent Methanol over a range of 4-20 μg/ml of AMLO and 5-25 μg/ml of HCT.


Kamble N, et al. (2004)\textsuperscript{16} developed method for determination and validation of second derivative UV-spectrophotometric method for simultaneous determination of lisinopril and amlodipine from tablet dosage form using ZCP: 256 nm of AMLO and 216 nm of LIS, Methanol is used as solvent over range of 5-30 μg/ml of AMLO and 10-60 μg/ml of LIS.

Sahu R, et al. (2006)\textsuperscript{17} developed Simultaneous spectrophotometric determination of amlodipine besylate and atorvastatin calcium from their binary mixture by dual wavelength and zero absorbance measurement using 257.4 nm and 360 nm with methanol as a solvent over a range of 10-60 μg/ml of AMLO and 5-30 μg/ml of ATOR.

Singhvi I, et al. (1998)\textsuperscript{18} developed Visible spectrophotometric methods for estimation of amlodipine besylate form tablets using extractive colorimetry method which involve formation complex with Bromocresol green (BCG), Bromophenyl blue (BPB) and Methylene blue (MB)\textsubscript{λ\textsubscript{max}}: 409 nm for BCG and BPB, 668.2 nm for MB Solvent: chloroform over a range of 10-80 μg/ml.

Wankhede S, et al. (2010)\textsuperscript{19} developed Spectrophotometric and HPLC methods for simultaneous estimation of Amlodipine besilate, Losartan potassium and Hydrochlorothiazide in tablets using Wavelength range: 231.5-241.5 nm for AMLO, 249-
259 nm for LOS and 266-276 nm for HCT, Solvent used is Methanol over a Range of 5-25 μg/ml for AMLO and HCT, 10-60 μg/ml for LOS.

**Kakde R.B, et al. (2008)** developed Spectrophotometric Method for Simultaneous Estimation of Amlodipine Besylate and Bisoprolol Fumarate in Pharmaceutical Preparations using $\lambda_{\text{max}}$ 222 nm and 365 nm and Solvent used is Methanol (10%) over a range of 10-60 μg/ml of AMLO and BPF.

**2.2.1 Official method for CANDESARTAN CILEXETIL**

**Japanese Pharmacopoeia, 2010** suggested a method for estimation of Candesartan cilexetil Tablet using HPLC method where S.P: Octadecylsilyl silica gel (4 μm) (4.6 mm i.d x 150 mm length), M.P: Acetonitrile: water: acetic acid (57:43:1) Flow rate: Adjust such that retention time at 13 min, Detection: 254 nm, Injection volume: 10 μl was utilized

**2.2.2 Reported methods of CANDESARTAN CILEXETIL**


Charoo A, et. al (2009)\textsuperscript{26} proposed determination of Candesartan Cilexetil in Tablet Dosage Forms and Dissolution Testing Samples by First Derivative UV Spectrophotometric Method using wavelength 254 nm and used solvent methanol over a range of 5-50 \textmu g/ml.


Saila K.A, et. al (2007)\textsuperscript{28} proposed method for Biovalidation of an SPE-HPLC-UV-fluorescence method for the determination of Candesartan and its metabolite valeryl-4-hydroxy-valsartan in human plasma using S.P: RP C18 Atlantis 100 mm×3.9 mm column, M.P: Acetonitrile: 5 mM phosphate buffer ( 65:35 v/v) with 0.025% triethylamine, Flow rate: 1.3 ml/min, Detection: 254 nm.

2.3.1 Official methods of simvastatin
Indian Pharmacopoeia, (2010)\textsuperscript{29} proposed method for estimation of simvastatin in tablet dosage form using Stationary Phase: ODS bounded to porous silica (3 \mu m), Mobile Phase: Solution A: 50:40 (Acetonitrile:0.1%v/v ortho Phosphoric Acid) Solution B: 0.1% v/v ortho phosphoric acid in acetonitrile, Flow rate: 3.0 ml/min,Detection: 238 nm, Injection volume: 5 \mu l and gradient controlled system is used for time 0-4.5 min(A- 100%), 4.5-4.6(95:5), 4.6-8.0 (25-75) and 8.0 to 11.5 min (25-75) for Mobile phase A and B respectively.

2.3.2 Reported methods of Simvastatin
Wang L, et. al(2000)\textsuperscript{32} developed Second-derivative UV spectrometric determination of simvastatin in its tablet dosage form zero-crossing technique of second derivative UV measurement at 243 nm using methanol as a mobile phase and range of simvastatin selected is 5- 25ug/ml, using this method it produces the accurate repeatable and reproducible result.

Vineet S, et. al (2010)\textsuperscript{33} developed Simultaneous estimation method of simvastatin and metformin hydrochloride in bulk and solid dosage form using methanol as a solvent and The estimation of simvastatin was carried out at 247 nm while metformin hydrochloride was estimated at 232.2 nm by applying the simultaneous equation method.
Chhalotiya K, et. al (2009)\textsuperscript{34} developed method for estimation of Simvastatin and Ezitimibe in Pharmacutical dosage form by First order derivative spectroscopy method using ZCP of Simvastatin and Ezitimibe is 243.9 and 256.5 nm respectively in methanol. Linearity for both Simvastatin and Ezitimibe is 2-12 μg.

2.4 List of Reported method for Indapamide

Chen D, et al (2006)\textsuperscript{35} developed Simple, sensitive and rapid LC-MS method for the quantitation of indapamide in human plasma--application to pharmacokinetic studies by a A simple liquid-liquid extraction procedure was followed by injection of the extracts on to a C18 column with gradient elution and detection using a single quadrupole mass spectrometer in selected ion monitoring (SIM) mode. The method was tested using six different plasma batches. Linearity was established for the concentration range 0.5-100.0 ng/ml, with a coefficient of determination (r) of 0.9998 and good back-calculated accuracy and precision. The intra- and inter-day precision (RSD%) was lower than 10%, and accuracy ranged from 85 to 115%. The lower limit of quantification was reproducible at 0.2 ng/ml with 0.2 ml plasma.

Jain S, et. al (2006)\textsuperscript{36} describes the method developed is validated in human whole-blood matrix, with a sensitivity of 0.5 ng/ml as lower limit of quantification. The procedure for the extraction of indapamide and glimepiride as internal standard (IS) involves haemolysis and deproteniation of whole blood using ZnSO(4) followed by liquid-liquid extraction using ethyl acetate. The sample extracts after drying were reconstituted and analysed by LC-MS/MS, equipped with turbo ion spray (TIS) source, operating in the positive ion and selective reaction monitoring (SRM) acquisition mode to quantify indapamide in human whole blood. The mean recovery for indapamide was 82.40 and 93.23% for IS. The total run time was 2.5 min to monitor both indapamide and the IS. The response of the LC-MS/MS method for indapamide was linear over the range of 0.5-80.0 ng/ml with correlation coefficient, r>0.9991. The coefficient of variance (% CV) at 0.5 ng/ml was 4.02% and the accuracy was well within the accepted limit of +/-20% at 0.5 ng/ml and +/-15% at all other concentrations in the linear range. This method is fully validated for the accuracy, precision and stability studies and also applied to subject-sample analysis of bioequivalence study for 1.5mg sustained-release (SR) formulations.