Literature review

- **Khorsravan R et al (2005)** described effect of food or antacid on febuxostat pharmacokinetics and pharmacodynamics in healthy subjects. A delay of tmax was observed with both food and antacid. Point estimates (PE) and confidence intervals (CI) for T and R ratios/differences are shown below for febuxostat Cmax, AUC and sUA 24-hour mean concentration (Cmean, 24).

- **Mulford D et al (2005)** concluded that effect of febuxostat on pharmacokinetics of despiramine, a CYP2D6 substrate, in healthy subject. The increase in total exposure to DES and the concomitant decrease in the 2-HD/DES AUC ratio suggest that the metabolism of DES to 2-HD via CYP2D6 was mildly inhibited. However, this effect was not considered to be clinically significant. The incidence of adverse events was similar between treatment regimens with the majority being mild and moderate in severity.

- **Vernillet L et al (2005)** concluded that effects of age and gender on febuxostat pharmacokinetics, pharmacodynamics, and safety in healthy subjects. The overall incidence of study drug related adverse events (AEs) was lower in M than in F (13% vs 54%) and in Y than in E (25% vs 42%). The most common AEs were headache and constipation. The majority of AEs were mild in severity. Neither age nor gender had any clinically significant effect on the PK, PD, and safety of febuxostat. Therefore, febuxostat does not require any dose adjustment based on age or gender.

- **Khorsravan R et al (2006)** explained the pharmacokinetics, pharmacodynamics and safety of febuxostat, a novel non-purine selective inhibitor of xanthine oxidase, in a dose Escalation study in healthy subjects. Febuxostat was well tolerated at once daily doses of 10-240mg. There appeared to be a linear pharmacokinetic and dose relationship for febuxostat doses within 10-120mg range. Febuxostat was extensively metabolized and renal function and not seem to play an important role in its elimination from the body.

- **Khorsravan R et al (2008)** concluded the effect of age and gender on pharmacokinetics, pharmacodynamics and safety of febuxostat, a novel Non-purine selective inhibitor of xanthine oxidase. The unbound peak concentration and area under the concentration-time curve for febuxostat were higher in women as compared with men (31.5 vs 23.6
ng/mL and 62.8 vs 53.9 ng/mL) the differences were not considered clinically significant and could be largely accounted for by weight differences between male and female subjects.

Rees L et al (1991)\textsuperscript{17} has developed a procedure for the simultaneous assay of clebopride and its major metabolite N-desbenzyleclebopride in plasma has been developed. The method utilizes capillary gas chromatography-negative-ion chemical ionization mass spectrometry with selected-ion monitoring of characteristic ions. Employing 2-ethoxy analogues as internal standards, the benzamides were extracted from basified plasma using dichloromethane. Subsequent reaction with heptafluorobutyric anhydride produced volatile mono and diheptafluorobutyryl derivatives of clebopride and N-desbenzyleclebopride, respectively. The methane negative-ion mass spectra of these derivatives exhibited intense high-mass ions ideal for specific quantitation of low levels in biological fluids. Using this procedure the recovery of the drug and metabolite from human plasma was found to be 84.4 ± 1.5% (n = 3) and 77.4±4.7% (n = 3), respectively, at 0.5 ng/ml. Measurement of both compounds down to 0.10 ng/ml with a coefficient of variation of less than 10.5% is described. Plasma levels are reported in four volunteers up to 24 h following oral administration of 1 mg of clebopride malate salt.

Vijyaraj P et al (2009)\textsuperscript{18} has developed UV spectrophotometric method for determination of clebopride in pure and in pharmaceutical formulation. The absorption maximum at 263nm and obeys be's law in the concentration range 20-100 ug/mL. The slope and intercept of the equation regression line are 0.0106 and 0.0045 respectively.

Levesque D et al (2002)\textsuperscript{19} has developed method for determination of Cisapride and noncisapride in human urine by API 3000 LC/MS. Cisapride and Norcisapride were assayed from a concentration of 1.00 to 150.00 ng/mL and 0.87 to 130.00 ng/mL respectively using Clebopride as internal standard. The extraction was performed using Varian C8 1cc (100 mg) cartridges. The cartridges were conditioned with methanol and water. A 0.1 M ammonium acetate solution was added to the cartridges, followed by the ISWS and the sample urine. Cartridges were washed with buffer, a solution of Acetonitrile in water and water. Cisapride and Norcisapride were eluted using 1% NH3 in methanol. Chromatography was achieved on a Phenomenex Luna C18 analytical column. Total run time was 2.50 minutes for each injection. Positive ion mass spectrometry was used monitoring 466.2→184.1 m/z for Cisapride and 314.3→184.1 m/z for Norcisapride.
Maddock J et al (1988) determined a procedure for the analysis of clebopride in plasma using capillary gas chromatography-negative-ion chemical ionization mass spectrometry has been developed. Employing an ethoxy analogue as internal standard, the two compounds were extracted from basified plasma using dichloromethane. Subsequent reaction with heptafluorobutyryl imidazole produced volatile monoheptafluorobutyryl derivatives whose ammonia negative-ion mass spectra proved ideal for selected-ion monitoring. The recovery of clebopride from plasma at 0.536 nmol/l was found to be 85.5 +/- 0.9% (n = 3) whilst measurement down to 0.268 nmol/l was possible with a coefficient of variation of 7.9%. Plasma levels of the compound are reported in two volunteers following ingestion of 1 mg of clebopride as the malate salt.

Weinmann W et al (2007) has developed method for quantitation of angiotensin II receptor antagonists in human plasma by liquid-chromatography-tandem mass spectrometry using minimum sample clean-up and investigation of ion suppression by using column phenylhexyl reversed phase column (Luna phenyl-hexyl 50 x 2 mm I.D., 3.5 µm) in calibration curve range 8-250 ng/ml by applying Protein precipitation extraction method.

Tanayama S et al (2007) has developed method for characterization of conjugated metabolites of a new angiotensin II receptor antagonist, candesartan cilexetil, in rats by liquid chromatography/electrospray tandem mass spectrometry following chemical derivatization. In this method column C18 used for separation. The chromatographic parameters as mobile phase combination reported as Acetonitrile and water (0.05% triethylamine and 0.05% acetic acid), also calibration curve range reported as 5–500 ng/ml.

Nevin E et al (2003) has developed method for Simultaneous analysis of candesartan cilexetil and hydrochlorothiazide in human plasma and dosage forms using HPLC with a photo diode array detector. The chromatographic parameter reported as column C18 (5 µm, 15 cm x 4.6 mm), Mobile phase: 10 mM potassium dihydrogen phosphate: methanol: acetonitrile (2: 80:18, v/v/v) (pH 2.5), Flow rate: 1.0 ml/min. The extraction method selected as Protein precipitation with calibration curve range 30.0–2500.0 ng/ml.
Jimenez R et al (2002)\textsuperscript{24} has developed fast screening method for the determination of angiotensin II receptor antagonists in human plasma by high-performance liquid chromatography with fluorimetric detection. The detector Excitation wavelength of 250 nm and an emission wavelength of 375 nm were selected. The extraction technique reported as solid phase extraction. The column used for separation was Bondapak C18 also mobile phase used as Acetonitrile–5 mM Acetate buffer (pH 4).

Himabindu V et al (2007)\textsuperscript{25} has developed Stability-Indicating LC Method for Candesartan Cilexetil by using CN column (250 mm × 4.6 mm), 5 μm, mobile phase Phosphate buffer (pH 3.0): Acetonitrile (50:50) with detection wavelength 210 nm.

Xiaoshan Z et al (2002)\textsuperscript{26} determined the content of candesartan cilexetil by using HPLC. The ODS column was used and mobile phase content Acetonitrile: Phosphate buffer (pH-3.2) (80:20). The detection wavelength was 252 nm. The calibration curve range reported as 0.5 ~ 2.5 μg.

Luo J et al (2004)\textsuperscript{27} determined candesartan cilexetil and its related substances by using HPLC. The mobile phase was prepared as KH2PO4 mixing with triethylamine (pH -5.8): Acetonitrile (48:52) and C18 column used with flow rate 1.0 ml/min. The wavelength was selected as 210 nm.

Chen Z et al (2004)\textsuperscript{28} has developed method for RP dissolution of Candesartan Cilexetil tablets and capsules. The C18 column used with mobile phase containing Acetonitrile: water: phosphoric acid: triethylamine (700:300:0.3:0.3). The detector length were selected 254 nm.

Erk N et al (2003)\textsuperscript{29} discussed application of first derivative UV-spectrophotometry and ratio derivative spectrophotometry for the simultaneous determination of candesartan cilexetil and hydrochlorothiazide. The calibration range 6.0–38.0 μg/ ml, 4.0–28.0 μg/ ml was selected for determination respectively. The first derivative amplitudes were 270.1nm, 255.5 nm respectively.

Mohammed J et al (2010)\textsuperscript{30} summarized the principle and the systematic way for LC-MS/MS bioanalytical method development. It explains the method development for phospholipids, chromatography conditions, incurred sample reanalysis.
- **Nair A et al (2010)**\(^{31}\) reviewed regarding bioavailability and bioequivalence studies which is useful for the applications of the bioanalytical method development. For regulatory submission bioavailability and bioequivalence studies are required to ensure therapeutic equivalence between a pharmaceutically equivalent test product and a reference product. Several methods are available to assess equivalence, including comparative bioequivalence studies, in which the quantitative determination of a drug substance or its metabolite is measured in biological matrix.

- **Wal P et al (2010)**\(^{32}\) reviewed chromatographic techniques. Selection of a successful chromatographic separation depends upon differences in the interaction of the solutes with the mobile phase and the stationary phase. The literature also explained selection of column on the basis of analyte nature and different chromatographic parameter like retention time, flow rate on the basis of that selected column.

- **Nicola C et al (2007)**\(^{33}\) discussed about sample carryover and contamination is a major problem that can influence the accuracy and precision of liquid chromatography-mass spectrometry (LC-MS), and liquid chromatography-tandem mass spectrometry (LC-MS/MS) bioanalysis. To reveal carry over issue reduce matrix as much as possible, select powerful solvent for injector rinsing, optimize good composition of mobile phase, use proper tubing and valves, minimize sample introduction that cause sticky situation.

- **Rajpoot B et al (2011)**\(^{34}\) discussed on parameters of bioanalytical method validation with a documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality attributes. Bioanalytical methods validation and its regulatory requirements also explain in this review.

- **Kol P (2011)**\(^{35}\) reviewed advanced methods in sample preparation. The various types of sample preparation approaches are Solid-phase extraction, Liquid-Liquid extraction, Protein Precipitation. Also explain the parameter for selection of proper extraction method.

- **Zhang J (2010)**\(^{36}\) explained an integrated bioanalytical platform for supporting high-throughput serum protein binding screening quantification of small molecules using liquid chromatography/tandem mass spectrometry on a triple quadrupole mass spectrometer has become a common practice in bioanalytical support of in vitro adsorption, distribution, metabolism and excretion (ADME) screening.
- **Kalakuntla R (2009)** explained regulatory audit point view on quality assurance view for bioanalytical methods. The accuracy and all parameters observed by quality assurance which requires for any method development for the analysis of analytes in biological fluids.

- **Wells D (2003)** discussed on the sample preparation techniques for bioanalysis. He focuses on high throughput (rapid productivity) techniques and describes exactly how to perform and automate these methodologies, including useful strategies for method development and optimization. Each of these chapters describing high throughput sample preparation techniques: protein removal by precipitation; equilibrium dialysis and ultrafiltration; liquid-liquid extraction; solid-phase extraction; and various on-line techniques.

- **Sethi P (2001)** reviewed regarding how to select suitable internal standard which is used in preparation of samples for bioanalytical method validation. An isotopically labeled internal standard will have a similar extraction recovery, ionization response in ESI mass spectrometry, and a similar chromatographic retention time. Internal standard mainly added to a sample in known concentration to facilitate the qualitative identification and/or quantitative determination of the sample components.

- **Health Canada guidelines (2012)** described all validation parameters like selectivity, accuracy, precision etc. and their acceptance criteria.