LITERATURE REVIEW

- **Jemal M. et al (2010)** summarizes the principle and the road map for systematic LC-MS/MS bioanalytical method development. Author focus on the three themes that have recently emerged as phospholipids, incurred sample and sound chromatographic considerations. Explained strategies to reduce the bioanalytical risk associated with plasma phospholipids, a dual approach involving extraction and chromatography is recommended.

- **Wells D A (2003)** emphasizes on the current state-of-the-art in 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 online techniques.

- **Shah V. P. (2007)** through his article provides historical perspectives in the evolution and development of the Bioanalytical method validation (BMV) employed for the quantitative determination of drugs and their metabolites in biological fluids. This guidance, virtually in one form or another, has been adopted universally as a standard procedure for validating bioanalytical assays used for pharmacokinetic, bioavailability, and bioequivalence studies intended for regulatory submission.

- **Jemal M. et al (2003)** has developed and compared the performance of an enhanced resolution method against a unit resolution method under optimized mass spectrometric conditions, using a lower limit of quantitation that could be easily achieved by either method. Under controlled conditions, the two methods were essentially the same, demonstrating that the enhanced resolution method is as accurate, precise and rugged as the unit resolution method.

- **Rocci M L. et al (2007)** has attempted to outline an approach to incurred samples reanalysis as one additional measure of assay reproducibility that is reasonable, practical, and statistically based for evaluation of bioanalytical methods during sample analysis elements.
that are not present in the standards and quality control samples used during pre-study validation experiments.

- **Nicola C. Hughes et al (2007)**\(^{14}\) in his article author has proposed that carryover and contamination be assessed not only during the validation of an assay but also during the application of the method in a study. In this article, the potential risks of carryover and contamination in each stage of a bioanalytical method are discussed, to explain to the industry why this recommendation is being made.

- **Wei Zeng et al, (2004)**\(^{15}\) has developed and assessed to extend the lifetime of extraction columns of high-throughput liquid chromatography (HTLC) for bioanalysis of human plasma samples. In this method, a 15% acetic acid solution and 90% THF were respectively used as mobile phases to clean up the proteins in human plasma samples and residual lipids from the extraction and analytical columns.

- **Matuszewski B. K. et al (2003)**\(^{16}\) described in his article the experimental approaches for studying, identifying, and eliminating the effect of matrix on the results of quantitative analyses by HPLC−MS/MS are described in this paper. Using as an example a set of validation experiments performed for one of investigational new drug candidates, the concepts of the quantitative assessment of the “absolute” versus “relative” matrix effect are introduced.

- **Hong Mei et al (2003)**\(^{17}\) has described simple strategies to avoid matrix effects: (1) select the same brand of plastic tubes for processing and storing plasma samples and spiked plasma standards; (2) avoid using Li-heparin as the anticoagulant; and (3) try switching the ionization mode or switching to different mass spectrometers when matrix effects are encountered. These three strategies have allowed us to use protein precipitation and generic fast LC techniques to generate reliable LC/MS/MS data for the support of pharmacokinetic studies at the early drug discovery stage.

- **Jun Zhang (2010)**\(^{18}\) explained an integrated bioanalytical platform for supporting high-throughput serum protein binding screening quantification of small molecules using liquid chromatography/tandem mass spectrometry (LC/MS/MS) on a triple quadrupole mass...
A spectrometer has become a common practice in bioanalytical support of *in vitro* adsorption, distribution, metabolism and excretion (ADME) screening.

- **Heller D N. (2007)** has suggested technique for assessing matrix effects on quantitative atmospheric pressure ionization mass spectrometry (API-LC/MS) methods. A newly designed experiment has the aim of efficiently simulating the quantitative behavior of an LC/MS method as a function of the amount of co-injected matrix extract. Two sets of mixtures were prepared in different formats to study matrix effects as a function of analyte or matrix amount.

- **Joachim Schuhmacher (2003)** has done a comparison of matrix effects using either electrospray (TurboIonspray, TISP) or atmospheric pressure chemical ionization (APCI) indicated that APCI is less prone to matrix effects. TISP is usually the first choice of ionization technique since unknown thermally labile metabolites might be present in the plasma samples causing erroneous results.

- **Kalakuntla RR et al (2009)** explained quality assurance auditor view point for bioanalytical methods. Any method developed for the analysis of analytes in biological fluids must yield consistent results despite the variations in conditions during the course of a project.

- **Khan H et al (2012)** has developed and validated specific ultra-performance liquid chromatography/quadrupole time-of-flight mass spectroscopy (UPLC/Q-TOF-MS) method for the simultaneous determination of aceclofenac, paracetamol, and their major degradation products in tablets. Diclofenac and para-aminophenol as the potential degradation product of aceclofenac and paracetamol, respectively, were analyzed.

- **Pattan S. R et al (2009)** has developed economical reverse phase high-pressure liquid chromatographic method for the simultaneous estimation of Paracetamol and Eticoxib from pharmaceutical formulation. The method was carried out on an inertsil ODS,5μ, C8-3 column, with a mobile phase consisting of methanol: acetonitrile: phosphate buffer pH3.5 (40:20:40 v/v) at a flow rate of 1.0 ml/min. Detection was carried out at 242.
- Ophelia Q. P et al (2005)\textsuperscript{24} has developed a liquid chromatography/mass spectrometry method for simultaneous determination of paracetamol and dextropropoxyphene in human plasma. Both were extracted from 0.5mL of plasma using solid-phase extraction. The chromatography was performed using a Thermo Hypersil APS-2 Amino column (250mm×4.6mm, 5μm) with a mobile phase consisting of acetonitrile and 0.4% glacial acetic acid in water (20:80).

- Ji HY et al (2005)\textsuperscript{25} developed sensitive and selective liquid chromatography-tandem mass spectrometric (LC-MS/MS) method for the determination of piroxicam, meloxicam and tenoxicam in human plasma was developed. Piroxicam, meloxicam, tenoxicam and isoxicam (internal standard) were extracted from human plasma with ethyl acetate at acidic pH and analyzed on a Sunfire column with the mobile phase of methanol:ammonium formate (15 mM, pH 3.0) (60:40, v/v).

- Patil K. R et al (2009)\textsuperscript{26} developed method for quantitative analysis of lornoxicam (Lxm) in pharmaceutical dosage forms. Chromatographic separation of Lxm and its degradation products was achieved on a C\textsubscript{18} analytical column with 0.05% (v/v) aqueous trifluoroacetic acid–acetonitrile, 70:30 (v/v), as mobile phase. The flow rate was 1.0 mL min\textsuperscript{-1}, the column temperature 30 °C, and detection was by absorption at 295 nm using a photodiode-array detector.

- J. Joseph-Charles & M. Bertucat (1999)\textsuperscript{27} Simple and rapid isocratic HPLC method has developed for the simultaneous analysis of the non-steroidal anti-inflammatory drugs tenoxicam, piroxicam, meloxicam, and lornoxicam using isoxicam as an internal standard. The analyte was chromatographed using a Lichrosphere RP18 column, a Tris acetic acid buffer-tetrabutylammonium reagent-tetrahydrofuran-acetonitrile as the mobile phase, and UV detection at 360 nm.

- Young Hoon Kim et al (2007)\textsuperscript{28} Sensitive and selective (LC-ESI-MS/MS) method for the determination of lornoxicam in human plasma was developed. Lornoxicam and isoxicam (internal standard) were extracted from human plasma with ethyl acetate at acidic pH and analyzed on a Sunfire C\textsubscript{18} column with the mobile phase of methanol:ammonium formate (10 mM, pH 3.0) (70:30, v/v). The analyte was detected using a mass spectrometer, equipped with electrospray ion source. The coefficient of variation and relative error for intra-and inter-
assay at four QC levels were 0.7 to 4.2% and -4.5 to 5.0%, respectively. The recoveries of lornoxicam and isoxicam were 87.8% and 66.5%, respectively.

- Dhara J. Patel & Vivek P. Patel (2010)\textsuperscript{39} A simple, rapid and accurate High-performance thin-layer chromatography (HPTLC) method has established and validated for the simultaneous determination of paracetamol and lornoxicam in tablets.

- Tapan K Pal et al (2011)\textsuperscript{30} worked on simple, rapid and feasible high-performance liquid chromatographic method with ultraviolet detection for the quantitation of lornoxicam in human plasma. Sample was prepared by simple liquid-liquid extraction. The chromatographic separation was carried out in a Hypersil BDS, C18 column (250 mm $\times$ 4.6 mm; 5 \( \mu \)m particle size). The mobile phase was a mixture of 10 m mol phosphate buffer (KH\textsubscript{2}PO\textsubscript{4}) of pH 6.0 and acetonitrile (55:45, v/v) at a flow rate 1.0 mL/min. The UV detection was set at 290 nm.

- Christian Puozzo et al (2004)\textsuperscript{31} has developed a sensitive high performance liquid chromatographic method coupled with a fluorimetric detection was set up, validated and then used routinely of the drug. After liquid–liquid extraction, drug and its internal standard were analyzed by reversed-phase liquid chromatography (LC). The assay linearity was validated up to 1000 ng/ml. The limit of quantification was set at 5 ng/ml. Precision values (relative standard deviations) were lower than 5.4%, whereas the mean accuracy was higher than 95%. The extraction recoveries were higher than 70% for both milnacipran and the internal standard.

- Ebru Uçaktürk et al (2010)\textsuperscript{32} has developed and validated gas chromatography–mass spectrometry (GC–MS) method was presented for quantitative analysis of milnacipran (MNP) in human plasma. MNP was efficiently derivatized with N-methyl-N-trimethylsilyltrifluoroacetamide (MSTFA) before analysis.

- Olivier Heudi et al (2012)\textsuperscript{34} explains about fingolimod (Gilenya FTY720) recently approved for the treatment of multiple sclerosis in Europe and in the USA. In the present study, have developed and validated a rapid and sensitive liquid chromatography–tandem mass spectrometry (LC–MS/MS) method to simultaneously quantify FTY720 and FTY720-P in human blood simultaneous quantitative analysis of FTY720 and its metabolite FTY720-P.
in human blood by on-line solid phase extraction coupled with liquid chromatography–
tandem mass spectrometry.

- **Min Kyo Jeoung et al (2007)** established the sensitive and selective method for the
determination eperisone hydrochloride) in human plasma was developed and validated. The
procedure employed an internal standard and a solvent extraction step followed by
chromatography on a Xterra C$_{18}$ minibore column. Detection was by electrospray ionization
tandem mass spectrometry with multiple reaction monitoring. The mass transitions of
eperisone and tolperisone (IS) were m/z 260 → 98 and m/z 246 → 98, respectively. The
method has a limit of detection of 0.1 pg/mL for eperisone based on the three times signal-to-
noise value with a linear range from 0.01 to 10.0 ng/mL for the analyte. Extraction recovery
was on average 98.6±7.2% (SD) for eperisone.

- **Takeshi Saito et al (2010)** worked on rapid gas chromatography-mass spectrometry (GC-
MS) method for the analysis of eperisone in serum using monolithic spin-column extraction.
The linear concentration range for eperisone was 2-2500 ng/ml. The limit of detection was
found to be 0.5 ng/ml. The average extraction recovery range was 92.8-96.0%. The intra-
and interday relative standard deviations (RSDs) of the concentrations were less than 12.6% and
12.5%, respectively. The accuracy of this method ranged from 95.0% to 98.3%.

- **Poole CF (2003)**, **Yang L(2010)** and **Prashant Laxman Kol (2011)** et al provided
advanced methods in sample preparation. The various types of sample preparation
approaches are: Solid-phase extraction, Liquid-Liquid extraction, Protein Precipitation.

- **Sharma Devanshu et al (2010)** worked on Solid phase extraction (SPE) is the commonly
used technique for sample preparation to reduce both time and labor in bioanalysis. Further,
this paper also discusses about the matrix effect in LC-MS/MS analysis and how to reduce
matrix effect in method development.

- **Health Canada guidelines (2012)** describes all validation parameters like selectivity,
accuracy precision etc and their acceptance criteria. Selectivity should be evaluated to assess
the interference at the retention time of the analyte and Internal standard with predetermined
method conditions.
B.K. Matuszewski (2006) a simple experimental approach for studying and identifying the relative matrix effect (for example “plasma-to-plasma” and/or “urine-to-urine”) in quantitative analyses by HPLC–MS/MS is described. Using as a database a large number of examples of methods developed in recent years in laboratories, the relationship between the precision of standard line slopes constructed in five different lots of a biofluid (for example plasma) and the reliability of determination of concentration of an analyte in a particular plasma lot (or subject) was examined.