LITERATURE REVIEW

- **Vinod P Shah (2007)** explained the evolution of guideline on bioanalytical method validation and the historical perspective behind its evolution. The guidance has been universally accepted for confirming the reliability and reproducibility of any developed method.

- **Hopfgartner G et al. (2004)** reviewed different mass spectrometric ionisation techniques and the different effects the drug undergoes while passing through MS quadruples. The application of mass spectrometer MS3 mode in drug metabolism is also well explained. De novo sequencing application and fragmentation cascade using enhanced multiple charge mode and time delayed fragmentation are also well illustrated.

- **Erin Chambers et al. (2007)** demonstrated a systematic, comprehensive strategy that optimizes sample preparation and chromatography method to minimize matrix effects in bioanalytical LC/MS/MS assays. The author has detailed the different sample preparation techniques, evaluation of matrix effect and optimization of sample clean up to reduce matrix effect. He has summarized the techniques yield cleaner extracts thereby producing a most sensitive and robust analytical method.

- **Patel D et al. (2011)** reviewed choices of different buffers compatible for LC-MS/MS analysis. The author has explained the criteria considered while choosing buffer for mobile phase and additives to be added and its effect on separation of analyte. A guideline which is to be followed while optimizing buffer for mobile phase in any LC-MS/MS method is recommended.

- **Gary Siuzdak et al. (2003)** illustrated that LCMS instrument is an invaluable tool in pharmacokinetic behavioral studies. Mass spectrometer coupled with different separation techniques are well demonstrated for different applications. The improvements in bio distribution and elimination studies are also well illustrated using these sophisticated techniques through this article.

- **Jan F Van Bocxlaer et al. (2000)** emphasised the application of LC-MS in forensic toxicology and toxicology in general. The author detailed the application of mass spectrometric determination of drug abuse in trace quantities in forensic studies. It has also summarised the available method for quantification of the narcotic and abuse drugs using mass spectrometer.

Doxorubicin and its metabolites at pg levels. The method is successful in extracting the analyte and metabolite from the cell although a very high affinity interaction occurs between analyte and cellular constituents.

- **Ch. Krishnaiah et al. (2010)**\(^{22}\), through his paper has summarised a stability indicating method for the development of Valsartan using UPLC. The article demonstrates the use of UPLC to reduce the run time of analysis to a greater extent.

- **Gaikwad P V et al. (2010)**\(^{23}\), demonstrated the advantages of UPLC over HPLC. The decrease in particle size and efficiency of system improves the analysis in drastic manner giving rise to less solvent consumption, lower run time and cost effective method. The improved signal to noise ratio leads to improved sensitivity.

- **Swartz ME (2004)**\(^{24}\), presented the utility of UPLC over HPLC to widen the scope of analysis for a high throughput application. The article describes the application and chemistry of sub 2µ Acquity columns with UPLC for improved resolution, separation and sensitivity.

- **Taylor P J (2005)**\(^{25}\), explained matrix effect in biological matrices, its underlying causes, strategies to overcome matrix effect and parameters to consider during method validation to evaluate matrix effect. He summarises that the careful assessment of matrix effect and judicial use of sample preparation techniques coupled with adequate chromatography, LC-MS/MS would provide a robust analytical platform.

- **Patel K et al. (2010)**\(^{26}\), described the use of monolithic stationary phases for sample preparation and chromatography. The monolithic phase for solid phase extraction used as offline and online for selective separation of compounds is illustrated in the article.

- **Kole P L. et al. (2011)**\(^{27}\), reviewed recent developments in bioanalysis sample preparation techniques and updates the basic principles and theory and possibility of automation. The advantage and limitation of each preparatory technique is discussed.

- **Pranay Wal et al. (2010)**\(^{28}\), reviewed the basic principle of Mass spectrometer and describes different sample preparation technique used in bioanalysis. The author has provided guidance for method development and describes the different parameters to be considered for optimization of method. The validation parameters and criteria are also explained in this article.

- **Gregg A Immrie et al. (2009)**\(^{29}\), described commonly occurring problems in LC-MS. Although it’s a sophisticated instrument with high throughput delivery he has emphasized on
the common difficulties like carry over, analyte adsorption, endogenous compound related suppression and measures to be taken to minimize, avoid or to overcome these problems.

- **B. Haritha Reddy et al. (2010)**\(^{30}\), through this article has explained the theoretical considerations, advantages and applications of UPLC in all the pharmaceutical analytical fields. The advantages of resolution, speed and sensitive speed using UPLC are well illustrated using the calculative parameters.

- **May L. Chiu et al. (2010)**\(^{31}\), reviewed different approaches for dealing with sample matrix. He has detailed the challenges in managing the matrices like urine, blood, and saliva. Different sample preparation techniques used for these matrices are detailed.

- **Achille Cappiello et al. (2008)**\(^{32}\), described matrix effect as major limitation in quantitative analysis using electro spray ionization mass spectrometer. The article describes the significance on removal of matrix effect for developing an efficient method, by illustrating its effect on accuracy, linearity and reproducibility of analyte estimation from matrices.

- **Jadhav D H et al. (2012)**\(^{33}\), demonstrated the development and validation of bioanalytical method for the estimation of Raloxifene and its two metabolites in human plasma. The method utilizes UPLC with a linear gradient mobile phase and solid phase extraction for sample preparation. The different validation parameters followed are also detailed and the results indicate a successful application of methodology.

- **Dujuan Zhang et al. (2011)**\(^{34}\), described the method development and validation of Rosuvastatin estimation in human plasma. The developed method with a sensitive of 0.1ng/ml is illustrated for studying bioequivalence in Chinese volunteers.

- **Marlus Chorilli et al. (2011)**\(^{35}\), described a method for the quantitation of Mirtazepine, an antidepressant drug in human plasma. The method utilizes a reverse phase chromatography and LC-MS/MS for the estimation. Inexpensive liquid liquid extraction method applied is capable of the extraction of analyte for the quantification of levels up to 0.5ng/ml.

- **Rama Rao K et al. (2009)**\(^{36}\), reviewed the bioanalytical validation parameters, the protocols to be followed for validation and the acceptance criteria on a quality assurance audit perspective. The need of evaluation of additional parameters like anticoagulant effect and dilution integrity are emphasized to encounter different sample preparation situations.

- **Dharmendra Patel (2010)**\(^{37}\), reviewed the concepts of matrix effect in LC-MS/MS analysis. The author has detailed the ways to prevent matrix effect and the ways to overcome the
challenges. The need for controlling the matrix effect in estimation of drugs in biological matrix is also been explained.

- D Chandrapal Reddy et al. (2012)\(^{38}\), demonstrated the development and validation of Duloxetine estimation in human plasma. The method utilizes Xterra RP-8 column for chromatographic separation, liquid-liquid extraction for analyte extraction and LC-MS/MS for detection. A sensitive method of 0.1ng/ml quantitation limit is achieved.

- Mathew Ewles et al.\(^{39}\), presented the numerous challenges in estimation of therapeutic peptides and proteins in biological matrix. The high concentration of endogenous proteins and adsorption by highly abundant proteins and poor MS/MS challenges in analysing the targeted proteins in a pool of other peptides are detailed. Different sample preparation approaches for peptides and proteins from the endogenous compounds are well detailed by the author.

- Armin Buchwald et al.(2012)\(^{40}\), demonstrated the analysis of five immunosuppressant in human plasma out of which four drugs could be measured simultaneously and mycophenolic acid separately. This method finds its application in therapeutic drug monitoring. The author has used deuterated internal standard for minimizing the ion suppression effect while analysis. The complete lysis of erythrocyte is emphasized as a crucial role in determination of the immunosuppressant in whole blood for complete recovery of analyte.

- Shafeeque Ahmed et al. (2012)\(^{41}\), addressed the poor recovery issues of analyte from biological matrix due to the matrix effect challenges in ESI-MS. The method for diagnosing and evaluating of matrix effect and difficulties in removing the phospholipids from the samples are detailed. The use of Hybrid SPE precipitation solid phase cartridges as a solution for matrix effect, its mechanism in effective removal of phospholipid is defined in the article.

- Douglas M Fast et al. (2009)\(^{42}\), in the workshop report of incurred sample re analysis(ISR) has described the necessity of performing ISR. The authors have detailed the selection criteria for sample selection, procedure for evaluation of ISR and acceptance criteria for both small and large molecules.