A REVIEW ON HUMAN PLASMA FOR GROWTH OF A PROCESS FOR MEASURABLE WILLPOWER

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ABSTRACT

Bioanalytical chemistry is the determination of medicines substances in biological fluids like plasma, serum in terms of qualitative and quantitative analysis. It plays important role in evaluation of pharmacokinetic parameters which required for bioavailability and bioequivalence studies. The validation of developed method required to assure common level of quality therefore use of validated methods increased in current practice. Analytical methods plays important role in research and development of new product. The quality assurance and quality control are the main control parameters used in method development and validation. The chromatographic and spectrometric or spectroscopic methods are selected on the basis of their characteristics, features along with deficiencies. The selected method for determination must be gone through every stage of all validation parameters. Investigation of each stage must be determine in same procedural variables, same environment and same matrix which can affect analyte evaluation in biological matrix started from clinical sample collection to sample analysis. Method validation will be start after confirmation of complete method development. Full method validation will be start after promising results of method development because the method developer doesn't have idea about the actual method conditions during method validation. Method development mainly involves evaluation of different conditions as per analyte nature and optimization of those conditions accordingly.

1. INTRODUCTION

The important stages in method development are preparation of sample, separation of prepared sample by using chromatography, detection of separated sample by using suitable detection method. To start method development of newer analyte extensive literature survey required. After literature survey the primary importance given to summarized import points and determines the concept of future work. Literature survey information will be used to select instrument that is comfortable for analysis. This includes analyticalcolumn, high performance liquid chromatography system and detector system like Mass spectrometry. Another parameter is internal standard, select suitable internal standard as per analyte parameters. Also select suitable extraction method which will give high recovery, accuracy and precision along with economical as industrial prospective. Two factors mainly consider for determination of quality are recovery and standardization of method. Recovery of analyte into biological matrix is refers to response for total amount of analyte in the contained sample. Comparison between matrix content and pure solvent is nothing but relative recovery and the absolute recovery is nothing but true test of recovery. Another important parameter is selection of internals standard. Generally it consider on the basis of molecule nature and suitability of chromatographic methods. The coefficient of the analyte and the internal standard are very similar is the main assumption consider for selection of internal standard. Now a day's structural

isotope analogue of targeted analyte used as internal standard. The structural and isotopic analogue of analyte is added to the biological sample prior to sample pretreatment to calculate the area ratio between analyte and internal standard is back calculated against standard curve which determine the concentration of medicines. The selection of suitable instrument and there make is an important issue during method development. The difference between different makes of instrument is not surprising and should be considering for method development. Limit of detection and calibration curve are the most important parameters and it's necessary to determined prior to method development as it is platform for future method development work. As per US pharmacopeia limit of detection is nothing but lowest concentration of an analyte in a sample that can be detected but not necessarily quantitated and lowest limit of qualification is nothing but a sample can be determined with acceptable precision and accuracy and under the stated operation condition of the method. These parameters associated with signal to noise ratio. The signal is measured in blank plasma and measured from base line to peak of apex and divided by peak to peakThe calibration curve is determined between lowest concentration of analytic to the highest required concentration as per reported Cmax concentration. The minimum six concentrations are required to define relationship between analytic response and concentration and it should be reproducible at all stages of method. The more concentration may be required in case of nonlinear relationship. The most appropriate weighing factor is 1/x, 1/x2 commonly observed. Among the seven none zero standards at least five should be pass the criteria.

2. REVIEW OF LITERATURE

Grabowski B. et al (2006) explained the pharmacokinetic and pharmacodynamics results along with safety of medicines in a dose escalation study in healthy subjects. The research article concludes that medicines showing linear kinetics in arrange 10-120 mg and it is well tolerated in single dose 10 to 240 mg on daily basis.

Joseph R. N. et al (2008) explained about the pharmacokinetic and pharmacodynamics results along with safety in healthy subjects by considering age and gender effect. In the comparison of male and female study data the area under the concentration time curve and unbound peak concentration were higher in Female than male (31.5 vs 23.6 ng/mL and 62.8 vs 53.9 ng/mL).

Hande A. et al (2012) described liquid-liquid extraction technique for medicines from human plasma. The internal standard was used trandolapril. The column BEH C18, 50 mm X 2.1 mm, 1.7 µm was used for analysis and mobile phase was consisting of 0.1% formic acid: acetonitrile in 25:75 ratios. The method run time was 1.5 min. The method resulted LLOQ was 0.075 µg/ml.

Abdul M. A. et al (2011) described that the medicines was highly soluble in methanol so it was selected as the solvent system for the medicines. The linearity range for medicines at its wavelength of detection of 315 nm was obtained as 0.2–15 µg/ml. The LLOQ was resulted 0.5281 µg /ml.

Bhalekar. M. R. et al (2011) has developed a RP-HPLC method for medicines in bulk and pharmaceutical dosage forms. The column used as C18 column 250 x 4.6 mm, 5µm and mobile phase consisting of methanol: ortho-phosphoric acid in the ratio of 90:10 v/v. The flow rate was finalized 1ml per minute and detected by UV detector at 316nm. The run time was 5.28 min. The quantification range was 10-100 µg/ml.

Chitaranjan M. et al (2012) described separation of medicines by using C18 column. The mobile phase was consisted with sodium acetate buffer (pH 4.0): acetonitrile (40:60, v/v). The rate of flow was 1.2 ml per minute and ultraviolet detection at 254 nm. Linearity range was 0.1–200 µg/ml. The LLOQ was 0.0783 µg/ml.

Rama R. N. et al (2012) conducted chromatographic separation on Nucleosil C18 (250 x 4.6mm, 5µm) column by using 10 mM ammonium acetate buffer (pH 4.0 adjusted with 0.2% triethyl amine) and acetonitrile in the ratio (15: 85, v/v) as a mobile phase. The rate of flow was 1.2 ml per minute and it detected by UV at 275nm. The run time was 3.45 ± 0.05 min. The linearity range was 50.0 – 400.0 µg/ml. The LLOQ was 30.23 µg/ml.

Dongsheng O. et al (2010) explain method for medicines determination in plasma using by using itopride as an internal standard. The liquid–liquid extraction used as sample separation method. The chromatographic isocratic gradient mode was used. CAPCELL MG-III C18 (150 mm × 2.1 mm, 5 µm) column was used. The electrospray ionization was used along with MRM interface using the respective[M+H]+ ions, mass to charge ratio 373.9 →184.0 for clebopride, 359.9 → 71.5 for itopride. The linearity range was 69.530–4450.0 pg/ml.

Andrade A. S. et al (2011) validated method with a C8 (150 × 4.6 mm, 5 µm) column. The wavelength was selected 205 nm. The rate of flow was 1.1 ml/min. The mobile phase consisted with acetonitrile (MeCN) and orthophosphoric acid (OPA) 0.01% (v/v) with pH 3.0 in a ratio 28:72 and column oven temperature was 25 ± 1°C. The analysis were performed by using forced decomposition techniques and quantified by LC-MS/MS.

Himabindu V. et al (2008) explain that analysis done by using immobilized cellulose based chiral stationary phase chromatography. Mobile phase was consisted as n-hexane:ethanol:diethylamine (50:50:0.3, v/v/v). The rate of flow was 1.0 ml per minute. The elution time was ~15 min. The LLOQ for the (R)-enantiomer 0.07 µg. Injection volume was 10 µl.

Krishnaiah Ch. et al (2013) achieved chromatographic separation done by using Acquity UPLC BEH C18 column (100 x 2.1 mm, 1.7 µm). Flow rate was 0.3 ml/minand detected at 210 nm. The molecular ion peaks at mass to charge ratio 428.20, 425.20 and 281.30 for the acid (Impurity 4), oxidized (Impurity 6) and N-dealkylated (Impurity1) forms of darifenacin respectively.

Ganeswar M. et al (2012) achieved chromatographic separation done by using Enable C18G column (250mm × 4.6mm, 5µm). The mobile phase was made up of methanol: 10mM TBAHS (60:40, v/v).

rate of flow was 1.2 ml/min detected by photo diode array at 285 nm. Linearity range was 1.0–200 µg/ml.

Ashwinee K. S. et al (2011) has developed method for darifenacinhydrobromide absorbance at 286 nm. The linearity range was 10 to 100 µg/ml. The solutions were found to be stable for the various concentrations ranging from 10-100% at 30 and 60 minutes.

Aswani D. C., et al (2011) explained the method for darifenacinhydrobromide determination by using UV as detector. The Linearity range was 20.00-46.50µg/ml.

Nageswara R. P. et al (2013) described bioanalytical method for medicines in plasma by using carbamazepine as IS. Protein precipitation used as Extraction method. The chromatographic column was C18 and mobile phase consist with acetonitrile–0.5% formic acid buffer (60:40, v/v). Rate of flow was set 0.8 mL per minute. The calibration curve range was 50–15,000 ng/ml. Run time for analysis was 2.5 min.

Ashish M. et al (2012) has developed bioanalytical method for the determination of medicines in plasma. Acyclovir is used as internal standard. Water Oasis MCX 1cc/30mg cartridge was used for solid phase extraction. The chromatographic column was Inertsil ODS-3V (4.6 × 250 mm, 5µ). The mobile phase was prepared by the mixture of milli-Q water: acetonitrile: formic acid (30:70:0.3 v/v). The run time was 2.6 min. The product ion transition were monitored in MRM and positive ion mode. The linearity range was 0.200 to 16.000 µg/ml.

Andy D. et al (2012) evaluated the analysis of cycloserine. In this method normal phase used with silica hydride-based stationary phase and detected by mass spectrometry. Analyses done by using gradient as well as isocratic conditions.

Chen Y. et al (2012) described HPLC-ESI-MS/MS method with m/z 178.0/ 90.9. XTerra MS C18, 150 mm × 2.1 mm, 5 µm column was used for determination. Mobile phase was consisted of 20 mm ammonium formate and 0.5% of formic acid into methanol (25:75, v/v) with flow rate 0.3 mL.

3. Research Gap

The present study is confined to verify the status of the bioanalytical method defines the determination or quantification of analytic or medicines and their metabolites in biological matrices such as plasma, urine, and serum. For reliability it must be validated. Bio analytical method overall procedures involved collection of sample at clinical phase, processing of collected sample, storage ofcollected sample, and analysis of collected biological matrix for determination of medicines. Bio analytical method validation involves following major activities such as selectivity, accuracy, precision, recovery, sensitivity, and stability. The selective and sensitive bio analytical methods require for the creation of accurate pharmacokinetics, bioavailability, and bioequivalence of medicines data. Validated Bio analytical method is used for quantitative determination of medicines and their metabolites in biological fluids.

Following are the major reasons for the development of newer bioanalytical methods:

a. In literature method for determination of medicines is not available.
b. Unavailability of method in biological matrix.
c. In official pharmacopeias medicines or medicines combination method not available.
d. Due to the interference observed by the formulation excipients, as per formulation analytical methods may not be available for the medicines.
e. Due to different medicines in combination with other medicines, analytical method may not be available.
f. The available analytical method may require expensive reagents and solvents.

CONCLUSION

Electrospray ionization technique has proven effective in generating ions close to the protonated molecule with sufficient intensity to monitor quantitatively, accurately and selectively. The simplicity of these methods, use of rapid extraction, chromatographic separation, mass spectrometric detection and sample turnover rate make them attractive procedures in high-throughput bioanalysis of analytes. The methods were applied successfully to analysis and quantification of concentrations of analyses in plasma samples obtained for pharmacokinetic, bioavailability or bioequivalence studies after therapeutic doses. However further studies needed in the pharmaceutical field to build up more sophisticated bioanalytical assay methods for the quantification of drug[s] and/or its metabolite[s] in human biological matrix. I.e. Serum, tissue and urine.

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