IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 2, July 2022
Impact Factor: 6.252

Modern Trends in Analytical Method Development for Pharmaceutical Drug: Review

Ms. Radha S. Prayag[1], Mrs. Farheen Asif Budhwani[2], Karishma A. Nikose[3], Ms. Pallavi P.Sambarkar[4], Ms. Shaha Parvin[5]

Assistant Professor, Quality Assurance Department, SCT College of Pharmacy, Aurangabad, India[1]
Assistant Professor, Pharamceutics Department, Jagdamba Institute of Pharmacy And Research, Kalamb, India[2,3]
Lecturer, SDMVM's Diploma In Pharmacy Institute, Aurangabad. India [4]
Lecturer, Dr. Y. S. Khedkar College of Pharmacy, Aurangabad. India [5]

Abstract: *The process of drug development requires a suitable technique which helps the scientist to analyse the drug molecule in an accurate, precise, and easiest way. For the quantitative and qualitative assessment of drugs it is very important to identify the accurate method for method development. This study helps to understand the different analytical method available for the process of drug development which includes different chromatographic technique. As traditional techniques usually do not deliver the speed required, some unique approaches are required to enable workflows to function as designed so we discuss about the modern trend which are available, and implacable in all these methods to improve the analytical behavior of these techniques. This review article contains the brief summary modern techniques in analytical method development, and method validation. The latest trends in method development technique were useful to defeat errors in analytical techniques.*

Keywords: Analytical techniques, Modern trends, HPLC, MISER, method development, and validation

I. INTRODUCTION

In line with the developments in the pharmaceutical field, the product range is constantly being renewed and diversified. New analytical techniques need to be developed and validated for new pharmaceutical products [1].Analytical method includes use of a specific technique and stepwise instructions which are used in qualitative, quantitative analysis of a sample. When applying standard methods to new pharmaceutical productions /products, the standard test method should be optimized and characterized for user-specific applications and verified its suitability. To characterize the product, it is important to properly designate the method used in the test before relying on the data obtained.[2] Analytical method can be based on spectroscopy, chromatography, electrochemistry or a combination of those techniques. Analytical methods should be used in Good Manufacturing Practices (GMP) and Good Laboratory Practices (GLP) environments, and developed using the protocols and quality control criteria specified in Q2 (R1) in the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines. The basic fundamentals for analytical method development are as follows[3]: 1. The routinely qualified and calibrated devices; 2. Well documented methods; 3. Reliable reference standards. Experienced analysts 5. Appropriate sample selection and batch integrity; 6. Checking for any changes.[4]

II. METHODS

2.1 High Performance Layer Chromatography (HPLC)

High-Performance Liquid chromatography (HPLC) is that leading distinct separating instrument which is used for many aspects of drug manufacture and analysis. Compare to HPLC other techniques, such as thin layer, paper & column chromatography; though useful have never been totally satisfactory As HPLC is highly sensitivity and specific, it gives précised result. But, HPLC is broadly used for two reasons first for Qualitative and analysis of unknown mixtures and secondly for Mixture's separation for the later analysis. The separation mode depends totally on interacting relationship between the analyte, stationary Phase, mobile Phase [5] It relies on pumps to pass a pressurized liquid solvent containing the sample mixture through a column filled with a solid adsorbent material. Each component

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 2, July 2022
Impact Factor: 6.252

in the sample interacts slightly differently with the adsorbent material, causing different flow rates for the different components and leading to the separation of the components as they flow out of the column.[6]

2.2 High Performance Thin Layer Chromatography (HPTLC)

High performance thin layer technique (HPTLC) is the advance form of enhancing the Thin Layer Chromatography (TLC). This technique was worldwide used for the identification, estimation, and to check the analytical profile of drug molecules. [7] Due to its fast seperation action, and flexible nature it is able to analyze the number of drug components throughout the pharmaceutical field. The main advantage of this technique is to analyze the drug in a short period of time, easy to handle, or clean the samples of crude drug easily. Together with HPLC and GC it belongs to the micro-analytical methods, which play an important role in research and routine laboratories. HPTLC is the most simple separation technique available today to the analyst. With the help of this technique we can characterize the chromatogram with no time limit for a large number of parameters. [8]

2.3 Supercritical Fluid Chromatography(SFC)

Complementarily to liquid and gas chromatography, Supercritical Fluid Chromatography (SFC) is becoming an appreciated separation technique in science due to its capacity to provide fast, robust, and efficient analysis [9]. In addition, this technique is considered as green due to its low utilization of organic solvents [10] that are toxic, expensive, and harmful to environment. During the last decade, many improvements were brought to SFC instrumentation to make this technique well-suited with the majority of columns, including columns packed with sub-2 μm particles [11]. It is an ideal substitute for the separation of hydrocarbons comprising of 80–130 carbon atoms, as GC methods would result in sample cracking at high temperatures.[12]

2.4 On-Chip Liquid Chromatography

On-chip liquid chromatography (LC) refers to LC technology that is miniaturized to fit on a microchip to permit fast, high-throughput analysis, with small sample volumes and low reagent consumption. Four different on-chip LC approaches have been developed to date: use of open-tubular, packed-particle, monolithic, and pillar array columns. These methods have been applied to proteomics as well as the analysis of small molecules and drugs in various biological samples. The main separation mode for on-chip LC is currently the reverse-phase mode. Other separation modes such as ion exchange and size exclusion can be developed for analyzing many kinds of bimolecular, including protein and DNA. Chip-based LC-MS does not require connections between the column and mass spectrometer, which reduces extra column band broadening. In pharmaceutical analysis, MicroTAS using on-chip LC is not just faster and more efficient than LC separation, but also enables automation of the entire analytical process. Hence, this technique can overcome the limitations of current pharmaceutical analysis. [13]

2.5 MISER Chromatography

Multiple-injection in single run is a simple technique to perform high-throughput analysis where the whole experiment resides in a single chromatogram, simplifying the data analysis and interpretation. Multiple-injection techniques are shown to increase instrument throughput by up to 70% and to simplify data analysis, allowing hits in multiple parallel experiments to be identified easily[14].It is a variation of flow-injection analysis in which samples are analyzed by direct injection into an eluent flow provided by a liquid chromatograph. In combination with an autosampler, samples can be continuously injected allowing the rapid evaluation of their contents. The collection of results from multiple samples within a single chromatogram also allows for simple evaluation of data.[15] MISER chromatography both speeds up analysis time, typically to less than 1 min for each sample. The MISER approach is best suited for optimization workflows with large groups of samples containing different levels of the same principal components.[16]

2.6 Hyphenated Techniques

For the development of method the seperation technique based on the coupling seperation, and online seperation will acquire to develop a new method for drug analysis which is called as hyphenated techniques. From the past years in analytical research this method plays a major role for the advancement, development, and application of drugs in the

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 2, July 2022
Impact Factor: 6.252

pharmaceutical analysis. To increase the potential of drug analysis the following different hyphenated techniques were used:

1. Liquid chromatography-Nuclear magnetic resonance (LCNMR)
2. Liquid chromatography-Mass spectrometry (LC-MS)
3. Liquid chromatography-Infrared spectrometry (LC-IR)
4. Gas chromatography-Mass spectrometry (GS-MS)
5. Capillary electrophoresis-Mass spectrometry (CE-MS)
6. Liquid chromatography-Photodiode array-Mass spectrometry (LC-PDA-MS)
7. Liquid chromatography-Mass spectrometry-Mass spectrometry (LC-MS-MS)
8. Liquid chromatography-Nuclear magnetic resonanceMass spectrometry (LC-NMR-MS)
9. Liquid chromatography photodiode array-Nuclear magnetic resonance-Mass spectrometry (LCPDA-NMRMS).[17]

III. METHOD VALIDATION

Method validation is the process used to confirm that the analytical procedure employed for a specific test is suitable for its intended use. Results from method validation can be used to judge the quality, reliability and consistency of analytical results; it is an integral part of any good analytical practice.19]

3.1 Parameters for Method Validation

As per ICH guidelines typical validation parameters which should be considered are listed below:

- **Accuracy:** The accuracy of an analytical procedure expresses the closeness of result of test result obtained by that method to the true value. The accuracy of an analytical procedure should be established across its range. The ICH documents recommend that accuracy should be assessed using a minimum of nine determinations over a minimum of three concentration levels, covering the specified range (i.e., three concentrations and three replicates of each concentration).
- **Precision:** The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. It is normally expressed as % relative standard deviation. Precision may be considered at three levels: repeatability, intermediate precision and reproducibility.
- **Repeatability:** Repeatability expresses the precision under the same operating conditions over a short interval of time. Repeatability is also termed intra-assay precision. Repeatability should be assessed using:
  1. a minimum of 9 determinations covering the specified range for the procedure (e.g., 3 concentrations/3 replicates each); or
  2. a minimum of 6 determinations at 100% of the test concentration.
- **Reproducibility:** Reproducibility expresses the precision between laboratories. Reproducibility is assessed by means of an inter-laboratory trial. Reproducibility should be considered in case of the standardization of an analytical procedure, for instance, for inclusion of procedures in pharmacopoeias.
- **Specificity:** Specificity is the ability to assess unequivocally the analyte in the presence of components which may be expected to be present. Typically these might include impurities, degradants, matrix, etc.
- **Limit of Detection (LOD):** The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value. Limit is prescribed as percentage or as parts per million. The limit of detection will not only depend on the procedure of analysis but also on type of instrument.
- **Limit of Quantitation (LOQ):** The quantitation limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy. It is expressed as the concentration of analyte (e.g., percentage, parts per billion) in the sample. The S/N ratio should not less than 10.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 2, July 2022
Impact Factor: 6.252

- **Linearity and Range:** The linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample. A linear relationship should be evaluated across the range of the analytical procedure.
- The range of an analytical procedure is the interval between the upper and lower concentration (amounts) of analyte in the sample (including these concentrations) for which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy and linearity.
- **Ruggedness:** The ruggedness of analytical method is the degree of reproducibility of test results obtained by the analysis of the same samples under a variety of conditions such as different laboratories, different instruments, different lots of reagents, different temperatures, different days, different analysts etc. It is normally expressed as the lack of influence on test results of proportional and environmental variables of the analytical method. For ruggedness study, the concentration of analyte is measured using different parameters such as.
    - Different operator in same laboratory.
    - Different equipment in same laboratory.
    - Different source of segment and solution.
    - Different laboratory.
- **Robustness:** The robustness of analytical method is the measure of its capacity, to remain unaffected by small but deliberate variations in method parameters and provides an indication of its reliability during normal usage. Experiments are performed by changing conditions such as flow rate, temperature (± 5^0C), buffer pH (± 0.5), and ionic strength of buffers. The method must be robust enough to withstand slight changes and allow routine analysis of sample.[20]

IV. CONCLUSION

Nowadays, it is very important to develop a method with minimum errors, and to conquer the faulted errors in analysis some of modern analytical method techniques were available which includes advancement in automated development of HPLC,Supercritical Chromatography, On-chip Chromatography, Hyphenated Chromatography Multiple-Injection In Single Run Chromatoraphy. These improves the accuracy, precision, specificity, linearity, and range for the development, and validation of method. So, we concluded that the modern techniques for analytical method development and the process of method validation data is useful for analytical method development of pharmaceutical product.

REFERENCES

[1]. Rashmin. "An introduction to analytical method development for pharmaceutical formulations,Pharm Rev 2008; 6, p1-10.
[2]. USP, Current Good Manufacturing Practices for finished Pharmaceuticals, 21 CFR, Parts 210 and 211, US Food and Drug Administration.
[3]. Singh RK, Rathnam MV, Singh SJ, Vegesna RV. Determination of Camylofin dihydrochloride and Nimesulide in Pharmaceutical preparation by Gas chromatography. American Journal of Analytical Chemistry. 2011; 2(8):944.
[4]. M.E Swartz , I.S Krull ,Analytical method development and validation. CRC Press; 2018 Oct 3.
[5]. U. Beskan , S.T.Yildirim, E.A.Yapar, " An Overview Of Analytical Method Validation",Universal Journal Of Pharmaceutical Research. Volume 5, Issue 1, 2020.
[6]. F.Gritti,H. Fabrice; Y.Guiochon, K.Georges, "The van Deemter equation: Assumptions, limits, and adjustment to modern high performance liquid chromatography",Journal of Chromatography A,2013,p .2.
[7]. HPLC,SLR. Research and reviews. A review on chromatography with high-performance liquid. Journal of Pharmaceutical Anallysis, 2015;4, p.1-15.
[8]. R.K Singh, M.V Rathnam, S.J Singh, R.V Vegesna. "Determination of Camylofin dihydrochloride and Nimesulide in Pharmaceutical preparation by Gas chromatography", American Journal of Analytical Chemistry. 2011; 2(8)p.944.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 2, July 2022
Impact Factor: 6.252

[9]. S. Natesan, D. Thanasekaran, V .Krishnaswami, C. Ponnusamy " Improved RP-HPLC method for the simultaneous estimation of tranexamic acid and mefenamic acid in tablet dosage form", Pharmaceutical. Analysis. Acta. 2011; 2(1)p.115.

[10]. A. G. Perrenoud, L. Veuthey, and D. Guillarme, "The use of columns packed with sub-2 μm particles in supercritical fluid chromatography," TrAC—Trends in Analytical Chemistry, vol. 63, , 2014 p. 44–54.

[11]. C. J. Welch, N. Wu, M. Biba et al., "Greening analytical chromatography," TrAC—Trends in Analytical Chemistry, 2010, 29, pp. 667–680,.

[12]. Z. Ramia, A. Bakain, Y. Al-Degs, "Supercritical Fluid Chromatography of Drugs: Parallel Factor Analysis for Column Testing in a Wide Range of Operational Condition" ,Hindawi Journal of Analytical Methods in Chemistry Volume 2017,1.p.2

[13]. it is an ideal substitute for the separation of hydrocarbons comprising of 80–130 carbon atoms, as GC methods would result in sample cracking at high temperatures, Green Chemistry Letters And Review 2021,14p.642-646 .

[14]. M. Tsunoda , "On-Chip Liquid Chromatography",MDPI Encyclopedia 2022, 2,p. 617–624

[15]. W. Schafer, H. Wang,C. J. Welch, Multiple-injection high-throughput gas chromatography analysis, 13 June 2016

[16]. R. Sandra E. Rodriguez, High-throughput analysis of controlled substances: Combining multiple injections in a single experimental run (MISER) and liquid chromatography–mass spectrometry (LC-MS),ELSEVIER Forensic Chemistry Volume 5, September 2017, Pages 8-15

[17]. Christopher J. Welch, Xiaoyi Gong, Wes Schaefer, Edwin C. Pratt, Tanja Brkovic, Zainab Prizada, James F. Cuff and Birgit Kosjek, Tetrahedron:Asymmetry, 2010,21p. 1674-1681 .

[18]. S. Sharma, N. Singh, A. Ankalgi, A. Rana, M.S.Ashawat, "Modern Trends in Analytical Techniques for Method Development and Validation of Pharmaceuticals: A Review",journal of Drug Delivery & Therapeutics. 2021,11,p.121-130

[19]. ICH Harmonised Tripartite Guideline, Validation of Analytical Procedures: Text and Methodology, Q2 (R1). International Conference on Harmonisation, Geneva: 2005,1-13.

[20]. USP-NF, Validation of Compendial Procedures, General Chapters,2010; Vol.1, 2010, pp734-736.