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Review Article

Modern Trends in Analytical Techniques for Method Development and Validation of Pharmaceuticals: A Review

Shivani Sharma[1], Navdeep Singh*[2], Amar Deep Ankalgi[3], Arti Rana[4], Mahendra Singh Ashawat[5]

[1] *Department of Pharmaceutical Analysis and Quality Assurance, Laureate Institute of Pharmacy, Kathog, Jawalamukhi, Himachal Pradesh 176031, India*

[2] *Department of Pharmaceutics, Laureate Institute of Pharmacy, Kathog, Jawalamukhi, Himachal Pradesh 176031, India*

[3] *Professor and Head of Department of Pharmaceutical Analysis and Quality Assurance, Laureate Institute of Pharmacy, Kathog, Jawalamukhi, Himachal Pradesh 176031, India*

[4] *Assistant Professor, Department of Pharmaceutical Analysis and Quality Assurance, Laureate Institute of Pharmacy, Kathog, Jawalamukhi, Himachal Pradesh 176031, India*

[5] *Principal cum Director, Laureate Institute of Pharmacy, Kathog, Jawalamukhi, Himachal Pradesh 176031, India*

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*Address for Correspondence:

Navdeep Singh, Department of Pharmaceutics, Laureate Institute of Pharmacy, Kathog, Jawalamukhi, Himachal Pradesh 176031, India

Abstract

The process of drug development requires a suitable technique which helps the scientist to analyze the drug molecule is an accurate, precise, and easiest way. For the quantitative and qualitative estimation of drugs in analytical chemistry it is very important to identify the best method for method development. This study helps the author to understand the various analytical techniques available for the process of drug development which includes spectroscopy, chromatography, electrochemical techniques, electrophoretic, flow injection analysis, and hyphenated technique. All these methods contain different analytical process with a variety of separate techniques. Also, we discuss about the modern trend which are available, and implacable in all these methods to improve the analytical behavior of these techniques. In method development process the validation of document must be required in the form of accuracy, precision, specificity, limit of detection, linearity, and range is considered. So, this review article contains the brief summary of available analytical techniques, and the latest trend in method development, or the process of method validation, and development of method. The discussed methods in this review article were revealed by the scientist, and these techniques must require in new drug development process, which helps the person to utilize the potential of these techniques. Trend in the analytical chemistry to overcome the error in method development was necessary, and the latest trends in method development technique were useful to defeat errors in analytical techniques.

Keywords: Analytical techniques, Modern trends, Process of method development, and validation.

INTRODUCTION

In analytical chemistry the analysis of drugs is useful for the seperation, estimation, quantification of chemical compounds obtained from natural and artificial sources. These compounds are typically constitute upto one or more chemical compounds.[1] The process of analytical chemistry starts with two major categories includes qualitative and quantitative analysis. In qualitative analysis only the obtainable samples are estimated, and in quantitative analysis the total number of elements in a compound should be identified. For example; the analysis of wide variety of compounds or products is useful for the analysis of drugs, because it includes the life. Nowadays, large number of drugs has been introduced in market, and the demand of drugs is increasing day by day.[2] The newly invented drugs are a type of new variety or either they are modified version of available drugs. These drugs are introduced in reference with the marketed drugs, and available scenario in pharmacopoeia. The use of pharmacopoeia in the drug development was necessary to report about the better therapeutic agents for widrawal in the market. Some times during the development of drugs the analytical profile of drugs may not be present in pharmacopoeias. So, in that case for the development of new drugs, it is necessary to prepare the important analytical methods.[3]

During the development of drugs there are many compounds generated by inventors, and they can easily evaluate their structure, behavior, also helps to find the impurities in a compound. If the all the parameters have done to target the drug, then the bioassays of drugs will performed to find that

how it will work, and functions analytically. The sciencetist from the past years focused on the little molecules which are organic in nature, and also the compounds from natural or synthetic sources.[4]

For the analysis of these large or small molecules the various methods are useful for the analytical procedure which includes High Performance Liquid Chromatography (HPLC), High Performance Thin Layer Chromatography (HPTLC), Liquid Chromatography-Mass Spectrometry (LC-MS) etc. These analytical techniques are typically used for the detection of compounds by mass spectrometry, and other mentioned techniques.[5] A very useful techniques is high performance liquid chromatography (HPLC) was the important, and strengthened technique for the analysis of drugs. Also the liquid chromatography-mass spectrometry technique were important to analyze the pharmaceutical drugs, and useful in drug metabolism study. Also these techniques are useful for the analysis, estimation, and identification of pharmaceutical drugs containing impurities, and products which are degraded, or used to isolate, and characterize the drug's potential from various natural, and synthetic sources.[6]

For the development of method the various requirements are helpful for the analyst to develop the better, suitable, easy, and accurate method are:

- Data is required to solve any analytical difficulty
- Sensitivity is necessary
- It is important to work with accuracy
- Preferred range for the analysis of drugs
- Precision is required at the time of method development

The process of method development also includes the method validation process in which the documents are verified at the time of any method development process, to analyse the method the various requirements for the validation of documents are:

- Quality assurance
- Acceptance from the designated international agencies for product development
- Registration of pesticide or pharmaceutical products should be required
- The process of validation is only occurs when the acceptance is done by testing
- Also, the product should be validated when; the quality control department performs their necessary requirements.[7]

The discovery of newer drugs depends on the basis of available technologies which includes biotechnology, biomedical engineering, genes etc. In today time the developments of new drugs is occurred worldwide by many pharmaceutical industries, the over system of drug development is used when the discovery is completely satisfy the term of accuracy, precision, and post marketing surveillance. In the field of pharmaceutical industries there are huge types of novel drugs are introduced in the market, so to control and find their quality the analysis of drug was more useful. This review highlights the important tools, and techniques which have been useful for the analysis of drugs. To analyse the drugs the following terms should required for the development of drugs.[8]

- Less time for analysis is useful to maintain the economical conditions
- During the analysis the accuracy of compound must follow the instructions by pharmacopoeia
- Also, the selected method were precise, and selective

1 Analytical Techniques for Method Development

In analytical chemistry the quantitative and qualitative determination of drugs the various techniques were used with their accuracy for method development.[9] All the available techniques were enlisted in Figure 1.

1.1 Spectroscopic techniques

For the process of method development spectroscopic technique was the most important technique. In our pharmacopoeias this technique is based on the natural absorption of UV radiations, and other chemical reactions.[10] Spectroscopy is totally based on the quantitative measurement, properties transmission, and wavelength function. This method has been great advantage to save time, or expenditure of labor. Also, this technique has great precision, and accuracy. In pharmaceutical analysis this method was specially applied to analyze the dosage forms in pharmaceutical industries has been increased regularly.[11] Also, there are some aspects for the colorimetric methods include:

- Formation of complex reaction
- Process of oxidation, and reduction
- Effect of catalytic ions

1.2 UV-Visible Spectroscopy

The method ultraviolet visible spectroscopy is based in the energy, and radiation or excitation of electrons. In UV-Visible method excitation of electrons is due the energy light, and the region to determine the sample wavelength, and absorbance is in the range of 200 to 800 nm. The absorption were only occurs when the presence of conjugated pi-electrons was available.[12]

1.3 FTIR Spectroscopy

The infrared spectroscopy leads the absorption to his lower energy state, and that causes vibration, or excitation of some atoms, and molecules. The functional group, and the original peaks with regards the molecule were identified by this method, and it will helps the sciencetist to develop a new method.[13, 29]

1.4 Mass Spectroscopy (MS)

In mass spectroscopy the molecule samples were ionized by high energy electrons. The mass of each charge were accurately measured, and examined by the fluctuations of magnetic field, acceleration of electrostatic waves which maintains the precise weight of molecules.[14]

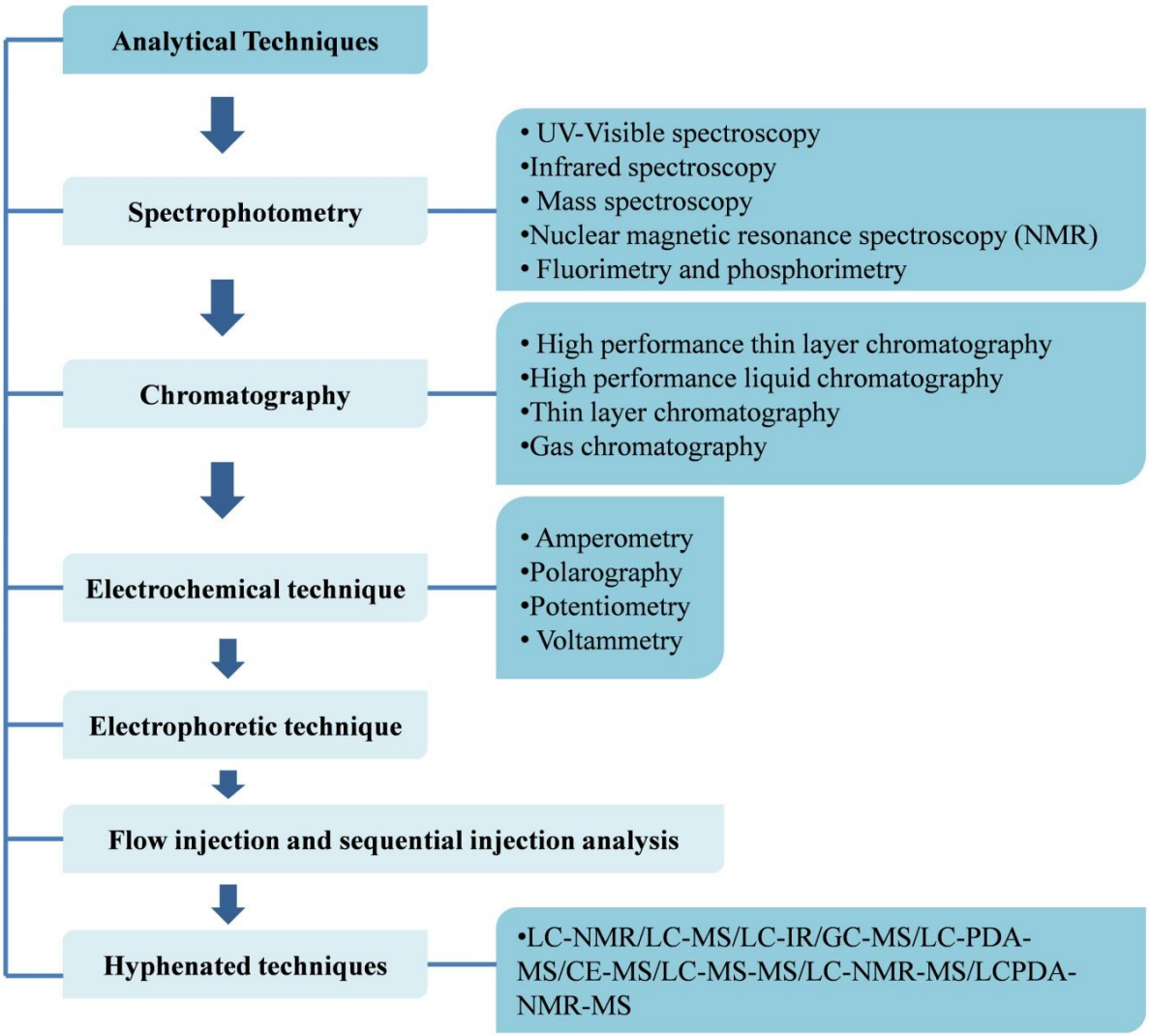

Figure 1: Available technique for method development

1.5 Nuclear Magnetic Resonance Spectroscopy (NMR)

From the past years many techniques are invented by sciencetist to overcome the analysis problems of new drug molecules. The nuclear magnetic resonance spectroscopy technique was used widely for the developments of drugs.[15] This technique was useful to identified, and to analyze the drugs by quantitative analysis for the determination of molecules. Also, the process of this method was helpful to characterize the drug composition, chemical products, and to determine the drugs used in pharmaceutical formulations, and biological fluids.[16]

1.6 Fluorimetry and Phosphorimetry

In our pharmaceutical industries fluorimetry and phosphorimetry techniques was incessantly growing for the analysis of micro samples. In fluorimetry technique the highly sensitive system was analyzed by without any loss in precision, and specificity of a method. In the previous studies there is a constant increasing rate in the application numbers was observed in fluorometry or phosphorimetry.[17] They represent these methods for the quantitative estimation of some drugs, which available in the form of biological fluids, and they were observed from past years.[18]

2 Chromatographic Technique

2.1 High Performance Thin Layer Chromatography (HPTLC)

This technique was globally used for the identification, estimation, and to check the analytical profile of drug molecules. It is a very advance technique, and it will be recognized as an major instrumental technique for drug analysis.[19] Due to its fast seperation action, and flexible nature it is capable 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. With the help of this technique we can characterize the chromatogram with no time limit for a large number of parameters.[20]

2.2 High Performance Liquid Chromatography (HPLC)

High performance liquid chromatography is a major technique which is used for the seperation of complex mixture of compounds and their molecules. The chemical compounds, and biological components are very effective to be encountered by this technique.[21] This technique was invented in the year 1980, and due to implementation of HPLC it will become the first method to analyze the assay of bulk drug materials from the USP-1980. Before the analysis of drugs HPLC method required starting their process in

terms of accuracy, precision, and wide range of samples were analyzed earlier than doing the HPLC. For the estimations of samples through HPLC an UV detector were used, and it is accomplished to find the wavelength of a sample. The process of UV detector will start only after the application of multiple programs of wavelength scanning.[22]

2.3 Thin Layer Chromatography (TLC)

Thin layer chromatography is a very old technique for the analysis of drugs in pharmaceuticals. In this technique the two phases were used one is known as mobile phase, and another one I known as stationary phase.[23] For the preparation of samples the phases includes solid phase, adsorbent, a thin layer of silica gel were spreaded over the plate of glass, and carry an aluminium support. This technique was widely used for the analysis of inorganic, and organic compounds. The compounds were analyzed by TLC due to its advantage over minimum cleaning; varieties of mobile phase selection, their flexibility, their capability to load the samples in high amount, and also this technique were cheaper in cost. Especially this method was used for the analysis of bulk drug components.[24]

2.4 Gas Chromatography

When we discus about the analytical techniques for drug analysis, a major method is in use for the pharmaceutical drug analysis is gas chromatography. This technique becomes a powerful technique for the excellent seperation of compounds which are volatile, and organic in nature. Gas chromatography allows the seperation o compounds for the quantitative estimation of multiple mixtures of drugs, which includes compound tracing, and the parts of compounds in per trillion. Gas chromatography plays an important role in the analysis of pharmaceutical drug products, and also useful to find out the impurities in pharmaceutical drug products.[25]

3 Electrochemical Techniques

The demand of electrochemical technique in pharmaceutical industries was increased in present time, or till from the past this method was in trend for the analysis of drug compounds. Furthermore, the varieties of samples are available in terms of drug analysis, and for the quantitative analysis of pharmaceutical components.[26] In recent developments the electrochemical techniques include amberlite XAD-2, nanoparticles of titanium dioxide, and carbon plate containing glassy carbon were applicable for the analysis of drugs like trimipramine, desipramine, and imipramine etc. To determine the electrochemical behavior of these compounds the following techniques were used like chronocoulometry, cyclic voltammetry, electrochemical impedence spectroscopy, and adsorptive strip pulse voltammetry.[27]

Table 1: Drug determination by a variety of electrochemical techniques

Applicable Technique	Drug determined	Electrode Used	Ref
Polarography	Ciclopirox olamine	Dropping mercury electrode (DME) or Static mercury drop electrode (SMDE)	28
	Anti cancer drug, Vitamin K3	Polished glassy carbon electrode (GCE)	
Potentiometry	Pentoxifylline	Multi walled carbon nanotube paste electrode	29
	N-acetyl-L-cysteine	Mercury film electrode	
Amperometry	Verapamil	Dropping mercury electrode	30
	Diclofenac	Carbon paste electrode	
Voltammetry	Leucovorin	Silver solid amalgam electrode	31
	Dopamine	Differential pulse stripping voltammetry	

4 Electrophoretic Technique

It is a very important technique for drug analysis in pharmaceutical fields, and the proper name of this technique is capillary electrophoresis (CE). Capillary electrophoresis technique is totally based on the electric charge ions by means of electromagnetic field. This technique was useful for the seperation, and analysis of drug components. During the process of electrophoresis the solute (sample) were pass through capillary to the detector, and the area of traveling the components of particular peak is directly proportional to the concentration of compound, and due to this phenomena the quantitative analysis of samples were performed by this useful technique.[32]

5 Flow Injection Analysis (FIA)

The flow injection analysis technique (FIA) was introduces by Ruzicka, and Hansen in US Denmark. This technique is based on the automatic experimentation of chemicals. So according to the study the authors revealed that the automation of chemical analysis is highly approached by FIA, and it is the main instrument used for the measurement or chemical analysis in the presence of chemical and physical equilibrium.[33]

6 Kinetic Technique of Analysis

The kinetic technique for analysis of various components in pharmaceutical was invented in year 1950, and it is used in automated instruments. The main implementation was made regarding the principle of kinetic technique which helps the sciencetist to chemical instrumentation process or highly applicable in the pharmaceutical drug analysis, data analysis, and method development. This method was completely based on the automatic system because the available techniques for drug analysis may stop their flow system, and the addition of reagent in a continuous way was also slow.[34]

7 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 pharmaceutical analysis.[35] The drugs were determined material from biological sources is the major analysis step for the invention of new drugs, and drug product development. To increase the potential of drug analysis the hyphenated techniques were used:

- Liquid chromatography-Nuclear magnetic resonance (LC-NMR)
- Liquid chromatography-Mass spectrometry (LC-MS)
- Liquid chromatography-Infrared spectrometry (LC-IR)
- Gas chromatography-Mass spectrometry (GS-MS)
- Capillary electrophoresis-Mass spectrometry (CE-MS)
- Liquid chromatography-Photodiode array-Mass spectrometry (LC-PDA-MS)
- Liquid chromatography-Mass spectrometry-Mass spectrometry (LC-MS-MS)
- Liquid chromatography-Nuclear magnetic resonance-Mass spectrometry (LC-NMR-MS)
- Liquid chromatography photodiode array-Nuclear magnetic resonance-Mass spectrometry (LCPDA-NMR-MS)

3. Modern Trends in Analytical Techniques for Pharmaceutical Drug Development

3.1 Automated Development in High Performance Thin Layer Chromatography (HPTLC)

High performance thin layer technique (HPTLC) is the advance form of enhancing the Thin Layer Chromatography (TLC). In HPTLC technique the process of automation in is helpful to surmount the size the droplets, and applied position of sample with the help of thin layer chromatography plate. In recent days, this technique will be the most effective tool due to its advantages over the reliability for the quantitative estimation of some analytes in microgram, and nanogram quantity.[36]

3.2 Development of Reverse Phase-High Performance Liquid Chromatography (RP-HPLC)

This technique is very simple, and useful for the identification of ATP, AMP, ADP, NADP+, NAD+, NADPH, AND NADH enzymes in erythrocytes of human body. The analysis of these enzymes were examined by reverse phase-high performance liquid chromatography by using supecosil LC-18 coloum of 5 µm, and detected with ultraviolet visible spectroscopy. Reverse phase-high performance liquid chromatography, and reverse phase chromatography contain stationary phase which is non polar, and aqueous in nature, or the mobile phase is polar in nature.[37]

3.3 Simultaneous analysis

In this article we report our work on the development and validation of the TLC Densito metric method for the simultaneous quantification of Bergenin, (+) - Catechin, Galicin, and Gallic Acid and quantification of ß-Sitosterol by HPTLC. Bioautography is a microbial detection method associated with flat chromatography techniques. It is mainly based on the antimicrobial or antifungal properties of the tested substances. LC-MS Method: LC / MS methods are suitable to a wide range of compounds of pharmaceutical interest, sensitivity, selectivity, speed of analysis and cost effectiveness. These analytical features have been continually improved, resulting in easier to use and more reliable tools.[38]

3.4 Automated injection technique

Automation is a key requirement in modern pharmaceutical analysis and quality control, as tringent Good Laboratory Practice (GLP) and Manufacturing Practice (GMP) regulations require in-depth analysis of large quantities of samples during all stages of the process, and manufacturing process of a pharmaceutical formulation.[39]

4. Analytical Method Development

When there is a definite technique, there are new methodologies that are released from an advanced product. These methodologies are optimized and valid through preliminary executions. Alternative ways of exchanging this procedure are planned and implemented within the laboratory comparative information with all the merits and demerits accessible.[40]

4.1 Need for method development

Drug evaluation shows the characterization and identity determination of drugs together in deiform and organic fluid form. This is a point of the production technique and development of a drug, the principal aim of analytical strategies is to get data regarding efficiency (which could be directly connected with the necessity of a identified dose), impurity (related to safety of the medication), bioavailability (consists of key drug traits like crystal kind, uniformity of drug and release of drug), stability (that shows the degradation product), and effect of producing parameters to verify that the assembly of drug product is stable.[41]

4.2 Criteria for the development of New Analytical Method

Pharmacological analysis is the basis for the finalization of the product. I most often, this is a temporary classification from the pharmacopoeia. Therefore, it is necessary to develop a new analytical method for obtaining these drugs.[42]

4.3 Steps involved in the development of the method

Documentation starts with the publishing process. It is more desirable to establish a system for complete documentation. All data relates to the studies must be recorder in the laboratories notebook or an electronic databases.[43]

4.4 Analytical characterization

1. All known information on the analytical and chemical properties of its structure.
2. Obtain the standard analysis (100% purity) .ii Arrangement much needed for proper storage (refrigerator, freezer dehydrator and freezer).
3. When multiple components are analyzed in the sample matrix, the number of components is indicated, the values are assembled and the availability of standards for each of the components is determined.
4. These methods are considered only if (spectroscopic, MS, GC, HPLC etc.,) are compatible with a wide stability.[44]

4.5 Methodological requirements

The primary requirements of an analytical method which are considered as analytical figures are defined. The limits of detection, selectivity, non-linearity, range, accuracy and precision required are defined.

4.6 Literature research and priority methodology

All types of bibliographic information related to the annual review were found. For synthesis, physical, and chemical properties, solubility, and relevant analytical methods, books, periodicals, chemical manufacturers, and regulatory agency compendia such as USP, NF, are reviewed. Chemical abstracts service (CAS) automated computerized literature searches are convenient.[45]

4.7 Choice of method

Using information in literature and printed matter, the methodology is adapted. The methods are changed as needed. Sometimes it is necessary to use an additional tool to produce, modify, improve the validation of existing methods for home testing and sampling.[46]

4.8 Instrumental setup and initial studies

Consumables have always been used (e.g. solvents, filters and gases). For example, the method never started on HPLC column that has been used earlier development. The standard analytic is suitable for injections / introduction is decisive for known concentrations and solvents are not prepared.[47]

4.9 Optimization

During optimization, changes in the parameters of conditions and conditions are isolated, that is, if it is an initial approach to diarrhea. Work has been done from an organized method cal plan, and every step is documented in case of dead ends.[48]

4.10 Documentation: Analytical figures of merit

The primarily determined analytical figures of timers are limit of quantitation (LOQ), limit of detection (LOD), linearity, time per analysis, cost, sample preparation etc., are documented. Evaluation of method development with real samples, and the solution sample can be a unique, absolute identification from an annual analysis of an interest by the components of other complex components.[49]

4.11 Determination of percent recovery of actual sample and demonstration of quantitative sample analysis

The validity of analytical method can be proved only by laboratory studies. Therefore, the documentation of this study is satisfactory to complete this type of study, it is a fundamental requirement to determine if the method is suitable for your applications.[50]

5. Development of the HPLC Method

High Performance Liquid Chromatography (HPLC) is one of the generally used analytical techniques. HPLC analyzed more than 85% of general pharmaceuticals. Russian Botanist M.S. Tswett in 190 was originally developed the technique of chromatography. HPLC is the separation module which contain mainly stationary phase and mobile phase has opposite polarity equipped with high-pressure pumps and a separation phase has been reached between two stationary phases and the mobile phase.[51]

5.1 Separation goals

The goals of HPLC separation need to be specified clearly are represented in Table 1.

Table.1. Separation goals in brief

Goal	Comment
Peak height	Narrow peaks are desirable for large signal/noise ratios
Resolution	Precise and rugged quantitative analysis requires that Rs be greater than 1.5
Solvent consumption	Minimum mobile phase use per run is desirable
Separation time	< 5-10 min is desirable for routine procedures
Pressure	< 150 bar is desirable < 200 bar is usually essential (for a new column)
Quantization	≤ 2% for assays ≤ 5% for less-demanding analyses ≤ 15% for trace analyses

5.2 Choice of the Column

Column are different from manufacture to manufacturer relative to its pore volumes, pore size, surface area, particle size, carbon load and whether they are end capped or not.

Table.2: Various types of columns and their applications

Column	Phase	Solvents	Application
Amino	Aminopropyl	ACN, MeOH, H_2O, THF, $CHCl_3$, CH_2Cl_2	Sugars, anions
Cyano	Cyanopropyl	ACN, MeOH, H_2O, THF	Ketones, Aldehydes
C8	Octyl	ACN, MeOH, H_2O	General, Nonpolar
C18	Octadecyl	ACN, MeOH, H_2O	General, Nonpolar
SAX	Aromatic quaternary amine	Salt Buffers, ACN, MeOH, H_2O	Anions

In the separation resolution, column length also plays a important role.[52] There are various types of column and the applications are shown in Table 2.

5.3 Adaptability for Automation

It is very important for the method to be "automatable", for methods that are likely to be used in a high sample volume application. To perform the manual sample preparation procedure should be easy. This will ensure the sample pre parathion can be mechanized in common sample preparation work stations.[53]

5.4 Understand the Chemistry

Similar to another research project, a global literature search of the physical and chemical properties of analytes, it is essential to ensure the success of the project.

5.5 Chemical Properties

It is very useful to appreciate the solubility and pKa of the analytes. Solubility in different organic or aqueous solvents resolves the best composition of the sample solvent. The pH in which the analyte will exist as a neutral or ionic species is determined by pKa. This information will provide a well organized example of schematic sample extraction and will determine the optimal method for achieving good separation in mobile phase.[54]

5.6 Potential degradation products

Subject to drug resistance conditions, API reproductively is commonly approved to ensure lower drug resistance under different conditions. Acidic pH, basic pH, neutral pH, different temperature and humidity conditions, oxidation, these are the various common stress conditions. These studies help determine if this substance is significant and related to method development and can also determine if the sample is a solvent resulting in dissolution of the best sample.[55]

5.7 Sample Matrix

Physical (e.g., solubility) and chemical (e.g., UV activity, stability, pH effect) properties of the matrix sample properties that will aid in an appropriate sample preparation scheme. For example, Hydroxypropyl Methylcellulose (HPMC) is a different solution for the delivery of absorbent and uniform water.[56]

5.8 Initial method conditions

The goal at this stage is to rapid development of HPLC conditions for subsequent method development experiments. Initial HPLC conditions are shown in Table 3.

Table.3. Initial HPLC conditions

Particle size	10 or 5 µm
Stationary phase	C_8 or C_{18}
Mobile phase	Buffer : Acetonitrile
pH of mobile phase	3 for neutral compounds 3 and 7.5 for ionic acidic 3 and 7.5 for ionic basic
Modifier	10 mM TEA and 1% HAS 1% HAS 10 mM TEA
Column length and internal diameter	250 mm x 4.6mm
Column temperature	Ambient to 35°C
Flow rate	1.5 - 2mL/minutes
Injection volume	10 – 25 µL
Buffer concentration	Phosphate 50 mM
% Buffer isocratic	50%
% Buffer gradient	20-80%

6 Method Validation

Method validation is used as a "final verification" of the method performance and could not be used as partly of the method development. Some typical method validation parameters can be extensively studied in the previous steps. In some cases, robustness can be completed in the final method optimization before validation of the method.[57]

At this point, your robustness experiments should be limited at any given time to the most important factors (usually less of these factors). As per ICH method validation can be defined as (ICH) "Establish documented evidence, which provides highly verifiable assurance that there is a specific activity that is consistent in a way that is consistent with the identification of lead time and its predetermined specification characteristics. An assay for a major component needs a different approach and acceptance criteria than a method for a trace impurity. A final method may be carried out at different sites around the world.[58]

6.1 Accuracy

The accuracy of a measurement is defined as the closeness of the measured value to the true value. In a method with high accuracy, a sample (whose "true value" is known) is an analytical analysis and the measured value is identical to the

actual value. Usually, the precision is presented and determines the precision of the recovery studies.[59]

There are some ways to determine accuracy:

1. Comparison of standard references
2. The analyte recovery spiked into blank matrix.
3. The analyte standard addition.

It should be released as the individual total impurities would be determined. For example, Weight/weight or area percent in all cases with respect to the major analyte.

6.2 Precision

The degree or the segmentation is defined by the individuality of the results when the procedures are applied repeatedly multiple samplings of a homogeneous sample. A more comprehensive definition given by the International Conference on Harmonization (ICH) differentiates precision into three types:

- Repeatability
- Intermediate precision
- Reproducibility

Repeatability is the precision of a method over a short period of time under the same operating conditions. Intermediate accuracies are official agreement, full measurements (including standards) when a method is applied multiple times within this laboratory. Reproducibility examines the precision between laboratories and is often determined in method transfer experiments or collaborative studies.[60]

6.3 Specificity/Selectivity

Selectivity and specificity of terms are often interchangeable. According to ICH, the term specific generally assign to a method that gives a response f or a single analyte only while the term selective assign to a method which gives response s for a number of chemical entities that may or may not be distinguished from each other.[61] The method is said to be selective, if the response is distinguished from all other responses. The term selectivity is usually more appropriate, since there are very few methods that respond to only one analyte. The analysis would have had to have interference from other strange external components and would have worked out well with them.[62]

A representative chromatogram or profile should be generated, and submitted to exhibit that the extraneous peaks either by addition of known compounds or samples from stress it sting are baseline determined from the parent analyte.[63]

6.4 Limit of detection (LOD)

Limit of detection (LOD) is the lowest concentration of analyte in a sample that can be detected, but not necessarily quantitated, under the stated experimental conditions. With the help of UV detectors, it is difficult to ensure the detection precision of low level compound due to potential gradual loss of sensitivity of detector lamps with age or noise level variation by detector manufacturer. Even low levels, a guarantee are needed that the limits of the LOD and LOQ limits can be reached by the estimated time method at any time.[64]

6.5 Linearity

The linearity of a method is a measure of how well calibration plot of response vs. concentration approximates gives a straight line. Linearity can be ensured by performing single measurements at different analyte concentrations. The data is then assessed using a linear least-squares regression. The resulting plot slope, correlation coefficient and intercept give the sufficient information on linearity.[65]

6.6 Range

The range of an analytical procedure is the interval between the upper and lower concentration (amounts) of analyte in the sample (including these concentrations). It is authorized by conforming that the analytical procedure gives an acceptable degree of linearity, accuracy and precision when applied to the samples that are containing amounts of analyte with zoriextremes of the specified range of the analytical procedure used.[66]

Conclusion

In the present study we examine the process of drug development which is based upone the analytical techniques. The methods for the development of drug are very accurate, and revealed by the scientists. The spectroscopy techniques for the quantitative and qualitative estimation of drugs have been includes the various methods UV-Visible spectroscopy, Mass spectrometry, Infrared spectroscopy, Nuclear magnetic resonance, Fluorimetry, and phosphorimetry. The process of seperation of drugs also depends on the chromatographic techniques includes High performance thin layer chromatography (HPTLC), High performance liquid chromatography (HPLC) which is an powerful seperation technique, and thin layer chromatography was useful for bulk drug screening, Gas chromatography to determines the impurities in pharmaceuticals. For the determination of drugs the electrochemical and electrophoretic technique were used. The electrochemical method helps the sciencetist to check the electrochemical nature of drugs by the use of voltammetry, chronocoulometry, pulse voltammetry etc. The capillary method in electrophoretic analysis of drugs was used for the quantitative estimation of drugs by applying electromagnetic field. To determine the flow system in a analytical process the flow injection analysis (FIA), and kinetic method were applies to justify the results. Hyphenated techniques for the analysis of drugs follow the various techniques in combination with two of three methods i.e; LC-NMR, LC-MS, LC-IR, GC-MS, CE-MS, LC-PDA-MS, LC-MS-MS, LC-NMR-MS, LCPDA-NMR-MS etc.

Nowadays, it is very important to develop a method with minimum errors, and to overcome the faulted errors in analytical chemistry some of latest trends in analytical techniques were available which includes advancement in automated development of HPLC, RP-HPLC, LC-MS etc. The steps involved in the process of method development, and their requirements provide suitable guidelines in addition to method development, and selection of method. These methods suggests the proper use of each technique in the better advancement of drug development process, which improves the accuracy, precision, specificity, linearity, and range for the development, and validation of method. So, we concluded that the available techniques for method development, recent trends, and the process of method validation or development revealed that the available data is useful in the process of analytical drug development, method development or validation.

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