

MODERN PHARMACEUTICAL ANALYTICAL TECHNIQUES: A REVIEW

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ABSTRACT

The process of drug development requires a suitable technique which helps the scientist to analyze the drug molecule in 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 applicable 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 separation, estimation, quantification of chemical compounds obtained from natural and artificial sources. These compounds are typically constitute up to 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 withdrawal 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 scientist 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.

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
- **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.

- **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
- **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

- **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 scientist to develop a new method.^{13, 29}

- **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

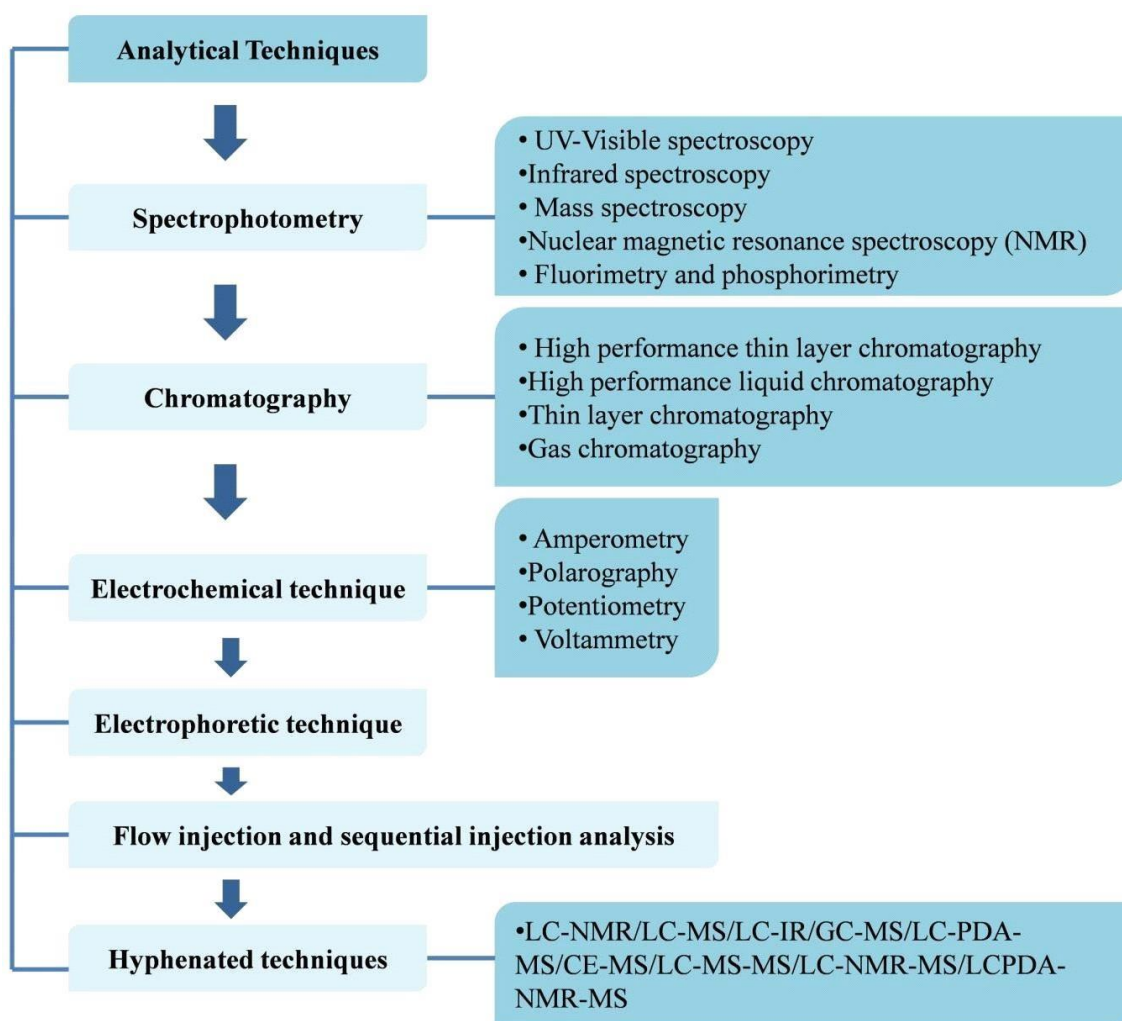


Figure 1: Available technique for method development

- **Nuclear Magnetic Resonance Spectroscopy (NMR)**

From the past years many techniques are invented by scientist 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 identify, 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

- **Fluorimetry and Phosphorimetry**

In our pharmaceutical industries fluorimetry and phosphorimetry techniques were 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 fluorimetry or phosphorimetry.¹⁷ They represent these methods for the quantitative estimation of some drugs, which are available in the form of biological fluids, and they were observed from past years.¹⁸

- **Chromatographic Technique**

- **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 advanced technique, and it will be recognized as a major instrumental technique for drug analysis.¹⁹ Due to its fast separation 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

- **High Performance Liquid Chromatography (HPLC)**

High performance liquid chromatography is a major technique which is used for the separation 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 was 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

- **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 is known as stationary phase.²³ For the preparation of samples the phases include 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

- **Gas Chromatography**

When we discuss 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 separation of compounds which are volatile, and organic in nature. Gas chromatography allows the separation of 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

- **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 impedance spectroscopy, and adsorptive strip pulse voltammetry.²⁷

- **Modern Trends in Analytical Techniques for Pharmaceutical Drug Development**

- **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 is helpful to surmount the size of 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

- **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 supacasil LC- 18 column of 5 μ m, 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

- **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 β -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

- **Automated injection technique**

Automation is a key requirement in modern pharmaceutical analysis and quality control, as stringent 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

Conclusion

In the present study we examine the process of drug development which is based upon the analytical techniques. The methods for the development of drug are very accurate, and revealed by the scientists. 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 suggest 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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