International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1177-1195 www.ijprajournal.com ISSN: 2456-4494

A Review on Analytical Method Development And Validation

Shravani S. More , Sandhya P. Kadam , Dr. Vivekkumar K.Redasani
YSPM's Yashoda Technical campus, Faculty of Pharmacy, Wadhe, Satara.

Date of Submission: 05-02-2025 Date of Acceptance: 15-02-2025

ABSTRACT
Analytical method development and validation are essential components in pharmaceutical, chemical, and biological research, ensuring accurate, reliable, and reproducible data for quality assessment and regulatory compliance. Method development involves selecting and optimizing analytical techniques to achieve accurate detection and quantification of target compounds under specific conditions. Validation establishes that the method meets critical parameters such as accuracy, precision, specificity, linearity, sensitivity, robustness, and reproducibility. These processes ensure compliance with international regulatory standards like ICH, FDA, and USP. This review provides an overview of method development strategies, key validation parameters, and their significance in pharmaceutical analysis, highlighting their applications in drug discovery, quality control, stability studies, and bioanalytical research, alongside advancements addressing contemporary analytical challenges.

KEYWORDS –Analytical method development, Validation, Regulatory compliance, Accuracy, Stability studies.

I. INTRODUCTION

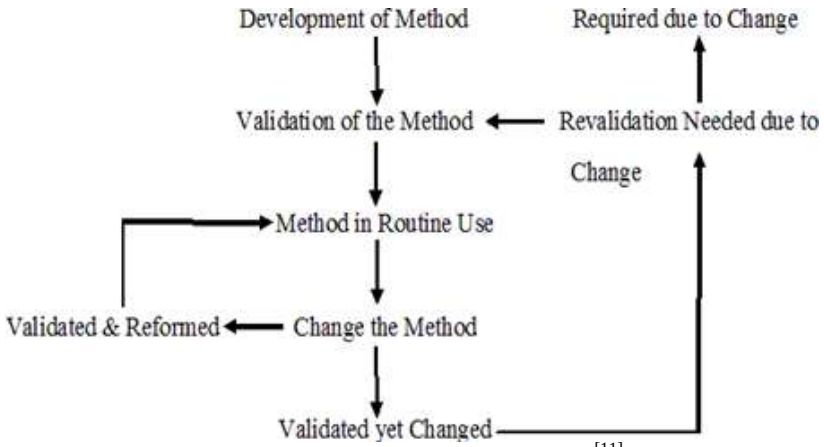
Quality control and quality assurance are the major areas in the pharmaceutical industry dealing with the analysis of materials starting from the raw material, intermediate products, APIS and finished products. Now and then new techniques are being developed all over the world. [1] The process of analytical 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] Development in scientific and concrete analytical methods has been resulted from the advancements of analytical instruments. The improvements of the analytical method development and analytical instruments have reduced the time and cost of analysis.[64] Various bioanalytical methods are also used.In this methods determine the drugs in biological fluid are becoming increasingly important for the study of bioavailability, bioequivalence (BE) Pharmacokinetics (PK) studies, quantitative evaluation of drugs, concentration and their metabolites, new drug development, research in basic biomedical and pharmaceutical sciences and therapeutic drug monitoring etc. [4] The data obtained from these methods is required in the pharmacokinetic and toxicokinetic studies of investigational new drug applications (INDs), new drug applications (NDAs) and abbreviated new drug applications (ANDAs). [5] International Conference On Hormonisation issued some guidelines for analytical method development and validation.and the processes work by this guidelines. [6] The reliability of an analytical finding is a matter of great importance to drive the formulation scientist in the developmental stage and impurity profile in stability study and dissolution data of the stability study as well as routine analysis. The importance of validation is producing reliable and repeatable results for routine analysis and stability analysis. This is especially true in the context of quality management and accreditation, which have become matters of increasing importance in analytical in dissolution[7] Pharmaceutical industry has focused on product Quality, Safety, and Efficacy. [8]The use of validated methods is important for an analytical laboratory to show its qualification and competency. [9]Analytical method validation is the systematic process of establishing that an analytical method is acceptable for its intended purpose. [10]

Analytical Method Development

When there are no definitive techniques are present, new methodologies are being progressed for evaluation of the novel product. To investigate the presence of either pharmacopoeial

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1177-1195 www.ijprajournal.com ISSN: 2456-4494

or non-pharmacopoeial product novel techniques are developed to reduce the value besides time for higher precision and strength. These methodologies are optimized and valid through preliminary runs. Alternate ways are planned and place into practice to exchange the present procedure within the comparative laboratory information with all accessible merits and demerits.



Life cycle of the analytical method [11]

Necessity of method development

Drug evaluation exhibits the identity characterization and resolution of the drugs in combination like dosage of analytical forms and organic fluids. At some point of producing technique and development of drug the principal purposestrategies is to generate data regarding efficiency (which might be directly connected with the need 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 manufacturing parameters to verify that the production of drug product is steady. [11]

Analyst before the event of latest technologies, don't forget below mention criteria:

→ is that this technique possesses the needful sensitivity?

→ is that this method sufficiently selective for direct use without interference employing the other element within the sample?

→ Are the accuracy and precision doable with this technique?

→ Are the reagents and equipment required on this method available or obtained at an inexpensive price?

→ is that the time requires to perform this system applicable?[12]

Analytical technique for technique development

There are various analytical techniques ae available for the analytical method development. [13]The analytical mehods provide more accurate and precise data not only supporting drug discovery and development but also the true data collection. [14] range of analytical methods that can be used in formulation design and development and focus onhow these systems can be applied to understand formulation components and the dosage form these build. [15]There are mainly two techniques for the method development-

1.Spectroscopic tecniques

2.Chromatographic techniques[16]

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1177-1195 www.ijprajournal.com ISSN: 2456-4494

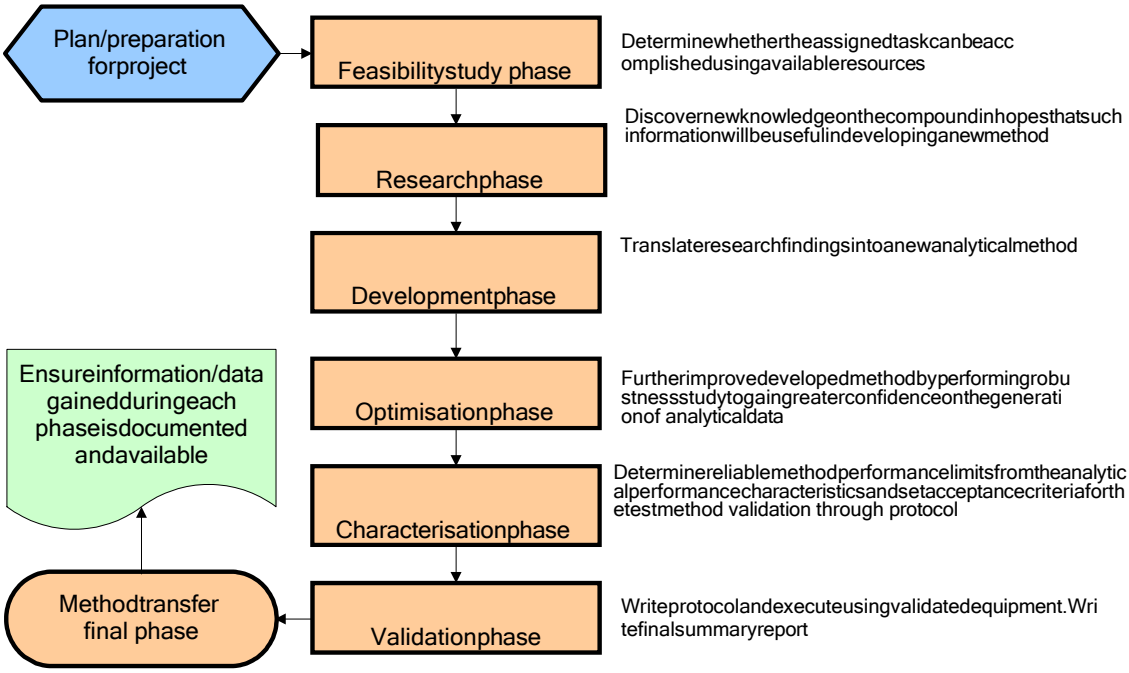


Figure 2 - Systematic approach in analytical method development and validation. [17]

1. spectroscopic techniques-

- UV spectroscopy
- Fourier Transform Infrared Spectroscopy
- Mass spectroscopy
- NMR[18]

This technique are described below:

- **UV spectroscopy:-**

❖ Spectroscopy: Spectroscopy is the measurement and interpretation of Electro Magnetic Radiation [EMR] absorbed and emitted when the molecules or atoms or ions of a sample move from one energy states to another energy states.[19]

❖ UV-VIS Spectroscopy: Ultraviolet (UV) spectroscopy is a physical technique of the optical spectroscopy that uses light in the visible, ultraviolet, and near-infrared ranges and it is based on Beer-Lambert law states that the absorbance of a solution is directly proportional to the concentration of the absorbing species in the solution and path length. Thus, for a fixed path length, it can be used to determine the concentration of the absorber in a solution. It is necessary to know how rapidly the absorbance changes with concentration, UV-VIS spectroscopy has been in general use for the last 37 years and over this period its become the most important analytical instrument in the modern day laboratory. In many application, other techniques could be employed but none rival UV-VIS spectroscopy for its simplicity, versatility, accuracy, speed, and cost-effectiveness. [20,21]

- **Fourier Transform Infrared Spectroscopy:-**

Infrared (IR) or Fourier transform infrared (FTIR) spectroscopy has a large operation range, from the analysis of small molecules or molecular complexes to the analysis of cells or tissues . [22] Fourier transform infrared (FTIR) spectroscopy represents a modern and popular technique that addressed IR spectroscopy as a powerful and reliable analytical technique.Recent FTIR technique developments rendered the tool as applicable to both quantitative and qualitative purposes of analyses. [23] An infrared spectroscopy measured the immersion of IR radiation made by each bond in the molecule and as a result gives spectrum which is commonly designated as %

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1177-1195 www.ijprajournal.com ISSN: 2456-4494

transmittance versus wavenumber (cm−1).[24]Fourier Transform Infrared Spectroscopy is based on the principle of vibrations. The types of vibrations in infrared (IR) spectroscopy include stretching and bending vibrations. [25]

- **Mass spectroscopy:-**

Mass spectrometry (MS) is a widely used detection technique that provides quantitative and qualitative information about the components in a mixture. [26] In qualitative analysis it is very important to determine the molecular weight of unknown compound and MS is capable of that. MS is also more sensitive than an UV detector for quantification. An MS detector consists of three main parts: the ionization source where the ions are generated, the mass analyzer, which separates the ions according to their mass to-charge ration (m/z), and the electron multiplier (detector). There are several types of ion sources, which utilize different ionization techniques for creating charged species. Three popular ionization techniques are: electrospray ionization (ESI). [27]Atmospheric pressure chemical ionization (APCI) and matrix-assisted laser desorption (MALDI). Electrospray is the most widely used ionization technique when performing LC-MS. [28-31]Mass spectrometer is also used with HPLC as detector. [32]

- **NMR**:

Nuclear magnetic resonance (NMR) spectroscopy is a very powerful tool to determine the structure of compounds.[33,34] This non-destructive spectroscopic analysis can reveal the number of atoms and their connectivity's, and thus the conformations of the molecules. Near infrared (NIR) spectroscopy is a quick, non-destructive method that is amenable for spot analysis application. In the last two decades, it has been increasingly used in pharmaceutical analysis [35]

2.Chromatographic techniques

- HPLC
- HPTLC
- TLC
- Gas chromatography

This techniques are listed below:

- **HPLC[High Performance Liquid Chromatography]:-**

High Performance Liquid Chromatography (HPLC) was derived from the classical column chromatography and, is one of the most important tools of analytical chemistry today. [36] 1 In the modern pharmaceutical industry, highperformance liquid chromatography (HPLC) is the major and integral analytical tool applied in all stages of drug discovery, development, and production. [37] HPLC is separation of each chemical entity from the sample mixture is based on its distinct affinity towards the adsorbent material in the column or the mobile phase, causing various constituents to travel at different velocities and separate. [38] The Goal of HPLC method is to try & separate, quantify the main drug, any reaction impurities, all available synthetic intermediates and any degradants. [39]HPLC is the most accurate analytical methods widely used for the quantitative as well as qualitative analysis of drug product and used for determining drug product stability.[40] The goal of the HPLC-method is to try & separate, quantify the main active drug, any reaction impurities, all available synthetic inter-mediates and any degradants.[41]The principle of separation followed is the adsorption of solute on stationary phase based on its affinity towards stationary phase. [42]Reverse phase chromatography is also plays an important role in the chromatography. [43]

Key features of HPLC:

- High resolution
- Small diameter, Stainless steel, Glass column
- Relatively higher mobile phase pressure
- Measured flow rate of mobile phase[44]

There are two phases are used normal phase and the reverse phase chromatography.[45]

- **HPTLC[High Performance Thin Layer Chromatography]:-**

High Performance Thin Layer Chromatography (HPTLC) is the most powerful advanced form of Thin Layer Chromatography (TLC) and consists of chromatographic layers of utmost separation efficiency and the application of sophisticated instrumentation for all steps in the procedure include accurate sample application, standardized reproducible chromatogram development and software controlled evaluation [46] HPTLC is used to minimize the technique failure. [47] High Performance Thin-Layer Chromatography (or Planar Chromatography) is a modern separation technique, established worldwide and distinguished by flexibility, reliability and cost efficiency. [48]HPTLC is the most simple separation technique today available to the analyst. It can be considered a time machine that can speed your work and

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1177-1195 www.ijprajournal.com ISSN: 2456-4494

allows one to do many things at a time usually not possible with other analytical techniques. In many cases instrumental Thin-Layer Chromatography offers a more suitable solution and often it is used as confirmatory or alternative technique.[49]

Advantages of HPTLC over other chromatographic methods:

HPTLC is the most simple separation technique today available to the analyst. Usually it can be considered as a time machine that can speed our work and allows us to do many things at a time which is not possible with other analytical techniques. Some of the advantages of HPTLC are as follows:

- There is very less need of Internal Standard.
- Lower analysis time and less cost per analysis.
- HPTLC is very simple to learn and the instrument is very easy to operate.
- In HPTLC, the sample preparation is very simple.
- It involves very low maintenance cost.
- Solvents used in HPTLC needs no prior treatment like filtration and degassing.
- In HPTLC, solvents of annular grade are suitable.
- In HPTLC, the mobile phase consumption for sample is extremely low.
- In HPTLC, allows the use of corrosive and UV absorbing mobile phases. [50]

High-performance thin layer chromatography (HPTLC) based methods could be considered as a good alternative as they are being explored as an important tool in routine drug analysis. A major advantage of HPTLC is its ability to analyze several samples simultaneously using a small quantity of mobile phase; this reduces the time and cost of analysis. [51-53]

- **TLC:-**

TLC is an important method for qualitative and quantitative analysis of drugs because it indicates some advantages in comparison to HPLC and GC methods, which are listed below:
(i)TLC can be used in those situations when HPLC-UV and GC are not suitable, for example, absence of UV activity of examined compound (important for HPLC analysis) or when the absence of volatility (important for GC analysis) is observed;
(ii)in comparison to HPLC in the case of TLC the high purity and high concentration of examined samples are not required. Unlike HPLC there is no danger that the samples impurities influence column damage and its separation property;
(iii)TLC needs no expensive equipment and is easy to work in comparison to HPLC and GC;
(iv)TLC allows a parallel separation and quantitative determination of many samples at the same time;
(v)it is possible to put on TLC plates a large volume of sample because the solvent excess removing during the sample is spotted on chromatographic plates.
For these purposes TLC greatly contributes to the analysis of different groups of drugs. [54]

- **Gas Chromatography:-**

Chromatographic separation methods are without any doubt the most frequently employed analytical techniques for compositional analysis. [55] Gas chromatography is a unique and versatile technique. In its initial stages of development it was applied to the analysis of gases and vapors from very volatile components. Gas chromatography is the analytical technique used for product identification (under very controlled conditions) and must be directly coupled to a mass spectrometer when information other than a comparative fingerprint (program) is required, such as positive identification of peaks on the chromatogram. [56]The basic principal of gas chromatography is that greater the affinity of the compound for the stationary phase, more the compound will be retained by the column and longer it will be before it is eluted and detected. Thus the heart of the gas chromatograph is the column in which separation of the component takes place, and to this must be added the source and control of the carrier gas flow through the column, a mean of sample introduction and a means of detection of the components as they elute from the end of the column. Since temperature will influence the volatility of the analytes, the column is placed in a thermostatically controlled oven.[57]Faster gas chromatographic separation is a generally beneficial option. Since the decrease time of analysis results in the increased sample. Reduction of analysis time can be achieved by changing column parameters: shorter length, smaller column inner diameter, thinner film of stationary phase, or operational parameters: faster temperature program rate, isothermal analysis. Different carrier gas, higher carrier gas flow rate or a combination of both approaches can be applied. [58]

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1177-1195 www.ijprajournal.com ISSN: 2456-4494

The following are the basic prerequisites for analytical method development

1. The devices that are routinely qualified and calibrated
2. Well documented methods
3. Reliable reference standards
4. Competent and experienced analysts
5. Proper sample selection and batch integrity
6. Checking for any changes. [59]

Method development commonly includes following steps:

1. Method development plan definition
2. Basic information collection
3. Standard analyte characterization
4. Determination of method requirements
5. Scientific article research
6. Method selection
7. Device installation and initial studies
8. Parameter optimization
9. Documentation of the analytical picture
10. Assessment of method development with sample implementation
11. Determination of percentage recovery of the sample
12. Demonstration of quantitative analysis for samples
13. Establishing the test procedure
14. Define method validation protocol
15. Validation of laboratory methods
16. Creation of validated test method
17. Validation report. [60]

Validation

Validation of an analytical method is the process by which it is established by laboratory studies, that the performance characteristics of the method meet the requirements for the intended analytical application. Validation is required for any new or amended method to ensure that it is capable of giving reproducible and reliable results, when used by different operators employing the same equipment in the same or different laboratories. The type of validation program required depends entirely on the particular method and its proposed applications.[61]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. Use of equipment that is within specification, working correctly and adequately calibrated is fundamental to the method validation process. Analytical methods need to be validated or revalidated:-

• Before their introduction into routine use
• Whenever the conditions change for which the method has been validated
• Whenever the method is changed[62]

Validation is derived from Latin from which means "strong ness". Validation is the strength or strongness of a procedure, process, and capability of an equipment to operate and is proved for its acceptability with confirmation and documented legally on the basis of scientific data. [63]Validation is the documented act of proving that any procedure,process,equipment,material, activity or system actually leads to expected result.[64]Quality engineering, Validation Manager, Production Manager and Speclist in validation Discipline which help to determination of written plan how to test a process and product quality The validation protocol is reviewed and approved by Head of Quality Assurance, Head of with specific reference criteria for ensuring product and process quality, safety and efficacy. The validation protocol implicates the following components for validation which may includes:-

1. Purpose and Scope of validation process.
2. Type of validation.
3. Total no of batches to be validated.
4. Validation team with qualifications and their responsibility.
5. Critical process attributes with their specifications.
6. Statistical tools used analysis of data.
7. Validated test method for raw materials and in process testing with specification.
8. Calibration and qualification criteria for equipment and process with specification.
9. Documentation of results, conclusion and approval of study results.[65]

Importance of validation

- Assurance of quality
- Process optimization
- Minimal batch failure and increased productivity
- Reduction in rejection
- Easier maintenance of equipment
- Increased output and product consistently
- Fewer complaints about process related failure
- More rapid innovation
- Ensures compliance with Regulatory standards
- Improve product quality and safety. [67]

When does validation begin?

Ideally validation starts in the very beginning, in the laboratory. In the lab, scientists

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1177-1195 www.ijprajournal.com ISSN: 2456-4494

discover exactly how the product reacts, as well as the parameters that are required to produce such a product. They learn under what conditions the product fails or becomes unstable, unusable and when its quality begins to suffer. Once the laboratory has established the boundary processing criteria, this information can then be used for establishing requirements for validation.

When does validation ends?

Validation of a system never truly ends. Once a new system and process have been validated the system still requires maintenance, periodic calibrations and adjustment. Therefore, the process is always under scrutiny and constant evaluation.[68]

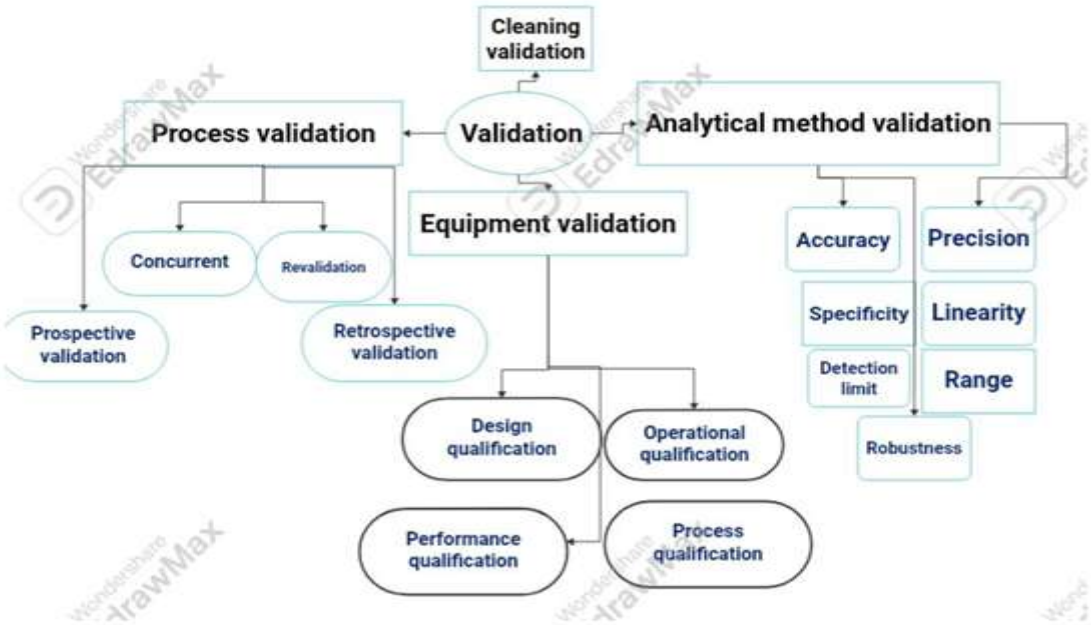
Criteria of Validation

The validation of an analytic method demonstrates the scientific soundness of the measurement or characterization. It is required to varying extents throughout the regulatory submission process. The validation practice demonstrates that an analytic method measures correct substance, in the correct amount and in the appropriate range for the samples. It allows the analyst to understand the behavior of the method and to establish the performance limits of the method.[69,70]

Need of Validation

Every day, a high number of HPLC analyses, related to the monitoring of organic compounds, are performed in thousands of laboratories around the world. These measurements are very useful in many situations: quality control of food and other consumer goods during manufacturing, processing, trading, and consumption, detection of deficient products or incorrect labelling, clinical assistance, checking the quality of drinking or waste water, forensic analysis in criminal investigations, and support for research, among others. In fact, every aspect of our life depends to some extent on analytical measurements. Many important decisions are taken on the basis of the results: batch release or refusal, purchase of a specific product, and trademark, prescription of a medical treatment, to permit the discharge of a water stream, the outcome of a trial, interpretation of the results, and so on. In all these cases, an incorrect value can lead to a wrong decision, with awful consequences for health, reputation, and economics. Besides, the cost of making these analyses is considerable, and on occasions, the decisions arising from the results may involve a significant dis bursement. Thus, it is important to determine the correct value and be sure of its reliability. For these reasons, the requirement for laboratories to use a validated method is now universally accepted. [71,72,73,74]

Types Of Validation



International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1177-1195 www.ijprajournal.com ISSN: 2456-4494

Introduction to process validation

Process validation is establishing documented evidences accomplished by validation team lead by quality assurance which collecting, analysing and evaluation of data from process design and manufacturing of a product for ensuring that process can reliably produce a product that meets predetermined quality specification. The purpose of process validation is every batch product be safe, effective and having good quality.[75] It is beneficial to manufacturer which deepens the understanding of process, maintaining consistency and reliability of product, decreases the risk of defect cost and regulatory Non-compliance it requires less in-process Controls and end-product testing.[76]

In the pharmaceutical industry, the purpose of process validation is to demonstrate that the manufacturing process consistently yields a product that meets its quality, safety, and efficacy standards. For this reason, the focus is primarily on controlling critical quality attributes (CQAs) and critical process parameters (CPPs)—those factors that directly influence the quality of the finished product. Process validation should confirm that the impurity profile for each API and finished product is within the limits specified.[77]

Process validation is widely practiced by pharmaceutical, biotechnological, medical device and herbal industries. The PV lifecycle concept links product and process development, the qualification of the commercial Manufacturing processes, and maintenance of the commercial production process in a coordinated Effort.Regulatory bodies continue to find firms for some finished product to have validated manufacturing processes. Manufacturing process validation is a process in which the process performance is constantly monitored and evaluated. The state of validation refers to the condition in which a pharmaceutical process consistently operates within predefined parameters, producing results that meet all quality, safety, and efficacy standards. To maintaining validated status of a process, measures must be taken that will allow any significant process changes to be recognized and resolved quickly. Such change control measures can apply to equipment, standard operating procedures, manufacturing instructions, environmental conditions or any other aspect of the process system that has an effect on its state of control and therefore on the state of validation.[78]

WHO:

Process validation is the collection and evaluation of data, throughout the product life-cycle, which provides documented scientific evidence that processes capable of consistently delivering quality products.[79

Scope of process validation

- It helps in reducing variability between different for ensuring uniformity in batch products adheres to quality criteria of purity, identity and potency
- It ensures high degree of quality of products within acceptance limits
- It maintain product integrity
- To demonstrate the robustness of the manufacturing process
- Process validation will ensure a robust product that is highly reproducible over time.
- Major changes after the initial validation will result in the need for subsequent Revalidation.
- To reduce the risk of defect costs and regulatory noncompliance.[80,81,82,83]

Advantages of process validation

- It expand real time monitoring that is checks process parameters like temperature,pressure,chemical concentration and adjustment is carried out if necessary for ensuring process stays within desired limits.
- It enhances data and evaluation capacities and increased confidence about process reproducibility and products.
- It enhanced reporting capability.
- It improve ability to set target parameter and control limits for routine production, correlating with validation results
- It is simple process and moisture sensitive,heat sensitive products can also be processed.
- Decreases the risk of preventing problems and thus ensure the smooth running of the process.
- Enhanced ability to statistically evaluate process Performance and product variables e.g. individuals; mean; Range; control limits.
- Process optimization: Optimization focuses on achieving the highest possible efficiency while maintaining quality standards. Optimize is “To Make as effective, perfect or useful as possible”. The Optimization of the facility, equipment, systems, and Processes plays vital role ensuring product comply with quality attributes leads to a product that meets quality

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1177-1195 www.ijprajournal.com ISSN: 2456-4494

standards at the lowest cost, balancing both effectiveness and cost-efficiency.

- Reduction of quality costs Quality costs are divided in to four categories. They are: A)Preventive costs .

B) Appraisal costs.
C) Internal failure costs
D) External failure costs.

By understanding and managing these categories of quality costs, organizations can optimize their quality control processes, reduce waste, and improve customer satisfaction.[82,84]

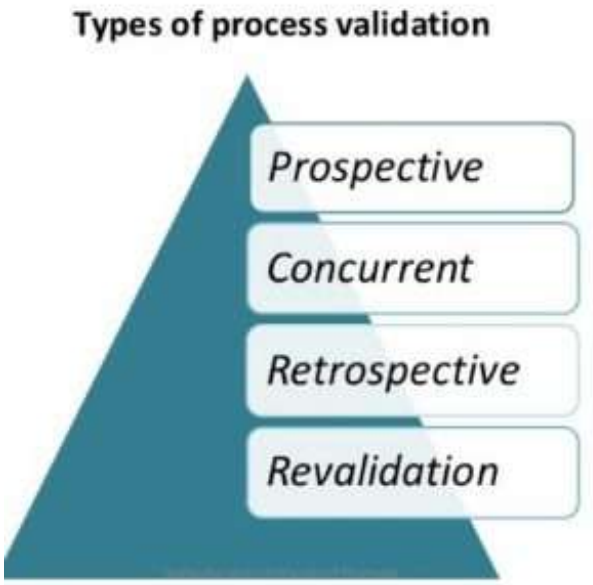
Reason for Process validation

The reasons for performing process validation can be summarized as:

- New product or existing products as per SUPAC changes.
- Change in site of manufacturing.
- Change in batch size
- Change in equipment.
- Change in process existing products.
- Change in composition or components
- Change in the critical control parameters.
- Change in vendor of API or critical excipient.
- Change in specification on input material.

Abnormal trends in quality parameters of Product through review during Annual Product Review (APR) .[85]

There are various types of process validation
This are listed below:-



Prospective validation

It is defined as the established documented evidence that a system does what it purports to do based on a pre-planned protocol.[86] This approach to validation is normally undertaken whenever the process for a new Formula (or within a new facility) must be Validated before routine pharmaceutical Production commences. It is used for facilities, processes, and process controls in operation use that have not undergone a formally documented validation process.[87]These experimental plan called the validation protocol is executed (following completion of the qualification trials) before the process is put to commercial use. Most validation efforts require some degree of prospective experimentation in order to generate validation support data. This phase is crucial before the process is officially put into commercial use.[88] This validation usually carried out prior to distribution either of a new product or a product made under a revised manufacturing process performed on at least three successive production sizes. The validation procedure involves running at least three consecutive production batches (full production scale) to demonstrate that the process consistently yields a product meeting quality, safety, and efficacy standards. Prospective process validation is executed After the completion of the R

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1177-1195 www.ijprajournal.com ISSN: 2456-4494

and D trial in Order to produce the product for the Commercial purpose.[89]Three batches are considered sufficient to demonstrate reproducibility and to confirm that the process performs as expected. Sampling data is consistent within each batch And across all three batches which demonstrates that The process performs in a robust and reproducible Manner capable of producing the drug substance.[90,91]

Concurrent validation

Concurrent validation is used to ensure that establishing documented evidence that process do what they purport to do, based on the information generated during process that is ,A process where current production batches are used to monitor processing parameter.[92]The concurrent validation process is similar to that of prospective validation. This method of validation can only be successful if the development stage has resulted in a proper understanding of the fundamentals of the process.[93,94] It is similar to prospective, except the operating firm will sell the product during the qualification runs, to the public at its market price, and also similar to retrospective validation.[95] Concurrent validation is used for establishing documented evidence that a facility and processes do what they purport to do, based on information generated during actual imputation of the process.[96]In special situations, where getting the medicine to patients quickly is very important and the benefits are greater than the risks, it may be allowed to start regular production without completing the usual validation checks first. This is known as concurrent validation.

Retrospective Validation

Retrospective Validation is defined as the establishment of documented evidence that a system does what it purports to do on review and analysis of historical information. The sources of such data are production ,QA and QC records. The issues to be addressed here are changes to equipment, process, specification and other relevant changes in the past.[86] Retrospective validation involves validating a process using historical data rather than performing a new set of experiments. It's commonly applied to processes that have been reliably used over time but may lack documented validation records. The main objective is to document evidence that a process consistently produces the desired outcome, even though it wasn't formally validated when initially implemented.Data from batch documents, process control charts, annual product quality review reports, maintenance log books, process capability studies, finished product test results, including trend analyses, and .[97] stability results acts as a source for retrospective validation. Data from a minimum of ten consecutive batches produced will acceptable for retrospective validation. In case if there are less than ten batches, which is not sufficient to demonstrate retrospectively then the retrospective validation should be supplemented with data generated with concurrent or prospective validation.[98]

Revalidation

It’s the repetition of validation process or part of it. This is carried out when there is any change or replacement in formulation , a equipment plan or site, location, batch size[99] and in cases where sequential batches fail to meet product specifications, revalidation is carried out to identify and resolve potential issues in the process, raw materials, or equipment. This is crucial for maintaining consistent product quality. [100] Even in the absence of any changes, periodic revalidation is carried out at specific intervals to confirm that the manufacturing process remains in control. This helps ensure continued compliance with regulatory standards over time. [101]Revalidation is may be categorized into two types.

- Revalidation in case of changes: After any change bearing on the product quality.
- Periodic revalidation: At scheduled intervals.[102,103]

Phases of validation

The activities relating to validation studies may be classified into three phases

- **Phase 1 Pre validation phase or the Qualification phase**
- **Phase 2 Process validation phase**
- **Phase 3 Validation Maintenance phase** [104]

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1177-1195 www.ijprajournal.com ISSN: 2456-4494

Parameters for method validation

Accuracy:

Accuracy is defined as the measure of exactness of an analytical procedure. It expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found. The ICH document on validation methodology recommends accuracy to be assessed using a minimum of nine determination over a minimum of three concentration levels covering the specified range (for example, three concentrations with three replicates each). Accuracy should be reported as percent recovery by the assay of known added amount of standard in the sample or as the difference between the mean and the accepted true value, together with the confidence intervals. Thus, accuracy of the method was studied by recovery experiments using standard addition method at three different levels (80%, 100% and 120.

Accuracy for analytical procedures is determined by two methods:

i) Absolute method
ii) Comparative method

i)Absolute method

The test for the accuracy of the method is carried out by taking varying amounts of the constituents and proceeding according to the specified instructions. The difference between the means of an adequate number of results and amount of constituent actually present, usually expressed as parts per hundred (%) i.e., % error. The constituent in question will usuall know the effect of these upon the determinations. This will require testing the influence of a large number of probable compounds in the chosen samples each of varying amounts. In few instances, the accuracy of the compound is controlled by separation (usually solvent extraction or chromatographic technique) involved .

ii) Comparative method

- In the analysis of pharmaceutical formulations or laboratory prepared samples of desired composition, the content of the constituents sought determined by two or more (proposed and official or reference) 'accurate' methods of essentially different character can usually be accepted in the absence of an appreciable formulation either in the proposed or reference methods comprising of various operations which include sampling, preparation of solution, separation of interfering ingredients if any and the method for the quantitative assay . [105]

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1177-1195 www.ijprajournal.com ISSN: 2456-4494

Precision:

The precision determines the closeness of agreement (degree of scatter) between a series of measurements attained from multiple sampling of the standardized sample under the prescribed conditions. The precision of an analytical method is normally expressed as the percent relative standard deviation for a statistically significant number of samples. The most common statistical terms employed is the standard deviation of a population of observation. Standard deviation is the square root of the sum of squares of deviations of individual results from the mean, divided by one less than the number of results in the set[106]

According to the ICH (International conference on harmonisation), precision should be accomplished at three different levels viz; repeatability, intermediate precision and reproducibility.

- Repeatability Repeatability is a measure of the precision under the same operating conditions over a short interval of time. It is sometimes denoted as intra-assay precision [107]
- Intermediate precision or Inter-day precision It is defined as the variation within the same laboratory. Typical parameters that are investigated include day-to-day variation, analyst variation, and equipment variation. [108]

Limits of detection and Quantitation:

The limit of detection (LOD) is defined as the lowest concentration of an analyte in a sample that can be detected, not quantified. It is expressed as a concentration at a specified signal:noise ratio,2 usually 3:1. The limit of quantitation (LOQ) is defined as the lowest concentration of an analyte in a sample that can be determined with acceptable precision and accuracy under the stated operational conditions of the method. The ICH has recommended a signal:noise ratio 10:1. LOD and LOQ may also be calculated based on the standard deviation of the response (SD) and the slope of the calibration curve(s) at levels approximating the LOD according to the formulae: LOD53.3(SD/S) and LOQ510(SD/S).[109]

Specificity:

Specificity is defined as the ability to access accurately and specifically the analyte in the presence of other components that may be expected to be present in the sample matrix. It is a measure of the degree of interference from such things like other active pharmaceutical ingredients, excipients, impurities and degradation products ensuring that a peak response is due to a single component only, that is no co-elutions exist. Specificity is measured and then documented in a separation by the resolution, plate count (efficiency) and tailing factor. This reserves the use of "specific" for those procedures that produce a response for a single analyte only. ISO/IEC most likely has the same understanding because it requires a method to be "selective" rather than specific. Our goal is to distinguish and quantify the response of the target compounds from the responses of all other compounds Selectivity is the ability to measure accurately and specifically the analyte in the presence of components that may be expected to be present in the sample matrix. Specificity for an assay ensures that the signal measured comes from the substance of interest, and that there is no interference from excipient and/or degradation products and/or impurities. Determination of this can be carried out by assessing the peak identity and purity. [109]

Linearity:

Linearity is the ability of analytical procedure to obtain a response that is directly proportional to the concentration (amount) of analyte in the sample. If the method is linear, the test results are directly or by well-defined mathematical transformation proportional to concentration of analyte in samples within a given range. Linearity is usually expressed as the confidence limit around the slope of the regression line

Range:

Range is defined as the interval between the upper and lower concentrations of analyte in the sample for which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy and linearity. [110]

Robustness:

The robustness of an analytical procedure is a 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. [111]

Ruggedness:

The ruggedness of an 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, analyst, instruments and lots of regents, elapsed assay times, assay temperature or days. Ruggedness

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 1177-1195 www.ijprajournal.com ISSN: 2456-4494

is a measure of reproducibility of test results under the variation in conditions normally expected from laboratory to laboratory and from analyst to analyst. [112]

Solution Stability:

Many solutes readily decompose prior to chromatographic investigations, for example, during the preparation of the sample solutions, extraction, clean up, phase transfer or storage of prepared vials (in refrigerators or in an automatic sampler). Under these circumstances, method validation should investigate the stability of the analytes and standards in solution form (in analytical preparations).

System suitability:

In addition, prior to the start of laboratory studies to demonstrate method validity, System suitability is considered appropriate when the RSD, theoretical plates, tailing factor and resolution parameters calculated on the results obtained at different time intervals, does not exceed more than of specified limit of the corresponding value of the system precision. [113]

System suitability test parameters and reccomendations
are given in below table :-

System Suitability Test Parameters and Recommendations [114]

Parameters	Recommendation
Theoretical Plates (N)	Should be > 2000
Capacity Factor (k')	The peak should be well-resolved from other peaks and the void Volume, generally k'>2.0
Relative retention	Not essential as long as the resolution is stated.
Resolution (R_s)	R_s of > 2 between the peak of interest and the closest eluting potential interferent (impurity, excipient, degradation product,internal standard) etc.
Tailing Factor (T)	T of </= 2
Repeatability	RSD </= 1% for N >/= 5 is desirable.

Guidelines: ICH , FDA , AOAC , USP , ISO 9000, and ISO 17025 It includes following: Q1A (R2): Stability Testing of New Drug Substances and Products (Second Revision).
Q1B: Photo stability testing of New Drug Substances and Products.
Q1C: Stability Testing for New Dosage Forms.
Q1D: Bracketing and Matrixing Designs for Stability Testing of Drug Substances and Drug Products
Q1E: Evaluation of Stability Data
Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV.
Q2A: Text on Validation of Analytical Procedures. [115]

II. CONCLUSION

Analytical method development and validation are fundamental components in ensuring the reliability, precision, and accuracy of analytical results in various fields, including pharmaceuticals, environmental science, and materials chemistry. Method development allows researchers to establish efficient, robust, and cost-effective procedures tailored to specific analytical needs. Validation ensures these methods meet predefined criteria for accuracy, precision, specificity, linearity, and robustness, providing confidence in their application for regulatory compliance and scientific integrity. The continued refinement of these processes, coupled with advancements in analytical instrumentation and software, will further enhance the quality and reliability of analytical data, supporting innovation and ensuring public safety.

REFERENCES:-

[1]. 1.Sudha, T., Krishana Kanth V., Nukala Poorana Chandra Sainath, Mishal, Saloman Raja T., and Ganesan V. "Method Development and Validation- A Review." Journal of Advanced Pharmacy Education & Research, vol. 2, no. 3, 2012, pp. 146-176. ISSN 2249-3379.

[2]. Sharma, Shivani, Navdeep Singh, Amar Deep Ankalgi, Arti Rana, and Mahendra Singh Ashawat. "Modern Trends in Analytical Techniques for Method Development and Validation of Pharmaceuticals: A Review." Journal of

Drug Delivery & Therapeutics, vol. 11, no. 1-s, 2021, pp. 121-130.

[3]. Ravisankar, Panchumarthy, Ch. Naga Navya, D. Pravallika, and D. Navya Sri. "A Review on Step-by-Step Analytical Method Validation." IOSR Journal of Pharmacy, vol. 5, no. 10, Oct. 2015, pp. 7-19. IOSR Journal of Pharmacy, www.iosrphr.org. (e-ISSN: 2250-3013, p-ISSN: 2319-4219).

[4]. Tijare, L.K., Rangari, N.T., and Mahajan, U.N. "A Review on Bioanalytical Method Development and Validation." Asian Journal of Pharmaceutical and Clinical Research, vol. 9, suppl. 3, 2016, pp.

[5]. Latha, Pushpa E., and Sailaja B. "Bioanalytical Method Development and Validation by HPLC: A Review." Journal of Medical and Pharmaceutical Innovation, vol. 1, no. 9, 2016, pp. 1-9.

[6]. Breaux, Jay, Kevin Jones, and Pierre Boulas. "Analytical Methods Development and Validation." Pharmaceutical Technology Analytical Chemistry & Testing, 2003, pp. 1-13.

[7]. 7.Geetha, G., Karanam Naga Ganika Raju, B. Vignesh Kumar, and M. Gnana Raja. "Analytical Method Validation: An Updated Review." International Journal of Advances in Pharmaceutical and Bio Sciences, vol. 1, no. 1, Jan.-Mar. 2012, pp. 64-71.

[8]. 8.Raman, N. V. V. S. S., Useni Reddy Mallu, and Hanimi Reddy Bapatu. "Analytical Quality by Design Approach to Test Method Development and Validation in Drug Substance Manufacturing." Journal of Chemistry, vol. 2015, Article ID 435129, 2015, pp. 1-8. Hindawi Publishing Corporation, doi:10.1155/2015/435129.

[9]. Taverniers, Isabel, Marc De Loose, and Erik Van Bockstaele. "Trends in Quality in the Analytical Laboratory. II. Analytical Method Validation and Quality Assurance." Trends in Analytical Chemistry, vol. 23, no. 8, 2004, pp. 535-552.

[10]. Chandran, S., and R. S. P. Singh. "Comparison of Various International Guidelines for Analytical Method Validation." Pharmazie, vol. 62, 2007, pp. 4-14.

[11]. Sharma, Shivani, Swapnil Goyal, and Kalindi Chauhan. "A Review on Analytical Method Development and Validation." International Journal of Applied Pharmaceutics, vol. 10, no. 6, 2018, pp. 8-15.

[12]. Sawale, Vilas Shivaji, and D. Umamaheshwari. "A Review on Novel Analytical Techniques Used in Method Development and Validation of Pharmaceuticals." Journal of Pharmaceutical Science and Research, vol. 12, no. 2, 2020, pp. 321-328.

[13]. 13.Siddiqui, Masoom Raza, Zeid A. AlOthman, and Nafisur Rahman. "Analytical Techniques in Pharmaceutical Analysis: A Review." Arabian Journal of Chemistry, vol. 10, suppl. 1, Feb. 2017, pp. S1409-S142

[14]. Attimarad, Mahesh, K. K. Mueen Ahmed, Bandar E. Aldhubaib, and Sree Harsha. "High-Performance Thin Layer Chromatography: A Powerful Analytical Technique in Pharmaceutical Drug Discovery." Pharmaceutical Methods, vol. 2, no. 2, Apr.–June 2011, pp. 71-75.

[15]. Müllertz, A., Perrie, Y., & Rades, T. (2016). Analytical techniques in the pharmaceutical sciences. Springer.

[16]. Ohannesian, L., & Streeter, A. J. (Eds.). (2001). Handbook of pharmaceutical analysis. Marcel Dekker. ISBN: 0-8247-0462-2.

[17]. Shabir, Ghulam. Evaluation and Application of Best Practice in Analytical Method Validation. Doctoral thesis, University of Sunderland, 2008, pp. 1–77.

[18]. Behera, Siladitya, et al. "UV-Visible Spectrophotometric Method Development and Validation of Assay of Paracetamol Tablet Formulation." International Journal of Pharmaceutical Sciences and Research, vol. 3, no. 12, 2012, pp. 4945–4953.

[19]. Analytical process of drugs by ultraviolet (UV) spectroscopy – a review R. Gandhimathi*, S. Vijay Raj, M.P. Jyothirmaie *Department of Pharmaceutical Analysis, SreeVidyanikethan College of Pharmacy, Tirupathi-517102, Andhra Pradesh, India

[20]. Skoog, D.A. Holler, F.J., Nieman, D.A., Introduction to UV Spectroscopy in, principle of instrumental\ analysis, 5thed., Cole publication, 2004.

[21]. Verma, Govinda, and Manish Mishra. "Development and Optimization of UV-Vis Spectroscopy: A Review." World Journal of Pharmaceutical Research, vol. 7, no. 11, 2018, pp. 1170–1180. ISSN 2277–7105.

[22]. Catherine Berthomieu , Rainer Hienerwadel , " Fourier transform infrared (FTIR) spectroscopy." Photosynth Res , 2009 , 101 , 157–170.

[23]. Khairi Mustafa Fahelelbom , Abdullah Saleh, Moawia M. A. Al-Tabakha, and Akram A. Ashames," Recent applications of quantitative analytical FTIR spectroscopy in pharmaceutical, biomedical, and clinical fields: A brief review." Reviews in Analytical Chemistry, 2022 , 41, 21-33,

[24]. Verma K , Akhtar MJ and Anchliya A," Combination of FTIR Spectroscopy and Chemometric Method on Quantitative Approach - A Review." Austin Journal of Analytical and Pharmaceutical Chemistry,2021, 8(1) , 1-15.

[25]. Maniar, Vishruti, Krishna Kalsara, and Umesh Upadhyay. "A Review of FTIR – An Useful Instrument." International Journal of Pharmaceutical Research and Applications, vol. 8, no. 1, Jan.-Feb. 2023, pp. 2486–2490. IJPRA Journal, ISSN 224

[26]. Mahatthanatrakul W, Pradabsang C, Sriwiriyajan S, Ridtitid W, Wongnawa M (2011) Bioequivalence of a Generic Quetiapine (Ketipinor) in Healthy Male Volunteers. J Bioequiv Availab 3: 108-113

[27]. Yasuhara A, Tanaka Y, Makishima M, Suzuki S, Shibamoto T (2011) LC-MS Analysis of Low Molecular Weight Carbonyl Compounds as 2,4-Dinitrophenylhydrazones Using Negative Ion Mode Electronspray Ionization Mass Spectrometry. J Chromatograph Separat Techniq 2:108

[28]. Ghosh C, Shinde CP, Chakraborty BS (2010) Ionization Polarity as a Cause of Matrix Effects, its Removal and Estimation in ESI-LC-MS/MS Bio-analysis. J Anal Bioanal Techniques 1:106.

[29]. Ghosh C, Gaur S, Singh A, Shinde CP, Chakraborty BS (2011) Estimation of Nevirapine from Human Plasma by LC-ESI-MS/MS: a Pharmacokinetic Application. J Bioequiv Availab 3: 020-025.

[30]. Ding MJ, Yuan LH, Li Y, Wang S, Wu XL, et al. (2011) Pharmacokinetics and Bioequivalence Study of \-037.

[31]. Ghosh C, Gaur S, Shinde CP, Chakraborty B (2011) A Systematic Approach to Overcome the Matrix Effect during LC-ESI-MS/MS Analysis by different Sample Extraction Techniques. J Bioequiv Availab 3: 122-127.

[32]. Toomula, Nishant, Arun Kumar, Sathish Kumar, and Vijaya Shanti Bheemidi. "Development and Validation of Analytical Methods for Pharmaceuticals." Journal of Analytical & Bioanalytical Techniques, vol. 1, no. 4, 2011, pp. 1–4. ISSN 2155-9872.

[33]. Afergan E, Najajreh Y, Gutman D, Epstein H, Elmalak O, et al. (2010) Drug Physical State and Fraction in Alendronate Liposomes. J Bioanal Biomed 2: 125-131.

[34]. Griffi ni P, James AD, Roberts AD, Pellegatti M (2010) Metabolites in Safety Testing: Issues and Approaches to the Safety Evaluation of Human Metabolites in a Drug that is Extensively Metabolized. J Drug Metabol Toxicol 1:102.

[35]. Ni Z, Feng YC, Hu CQ (2011) Analyzing the Methods to Remove Artifacts Encountered in the Development of a NIR Quantitative Model for Powder Medicines. J Anal Bioanal Techniques 1:114.

[36]. V. Gupta, A.D. K. Jain, N.S. Gill, K. Gupta, Development and validation of HPLC method - a review , Int. Res J Pharm. App Sci., 2(4) (2012) 17-25

[37]. Y. Kazakevich, R. Lobrutto, HPLC for Pharmaceutical Scientists, John Wiley & Sons, New Jersey, 2007.

[38]. Sahu, Prafulla Kumar, et al. "An Overview of Experimental Designs in HPLC Method Development and Validation." Journal of Pharmaceutical and Biomedical Analysis, vol. 147, 5 Jan. 2018, pp. 590-611.

[39]. M.S. Azim, M. Mitra, P.S. Bhasin, HPLC method development and validation: A review, Int. Res. J. Pharm. 4(4) (2013) 39-46.

[40]. B.V. Rao, G.N. Sowjanya1, A. Ajitha, V.U.M. Rao, Review on stability indicating hplc method development, World Journal of Pharmacy and

Pharmaceutical Sciences, 4(8) (2015) 405-423.

[41]. S. Sood, R. Bala, N.S. Gill, Method development and validation using HPLC technique – A review, Journal of Drug Discovery and Therapeutics 2 (22) 2014, 18- 24.

[42]. M.S. Charde, A.S. Welankiwar, J. Kumar, Method development by liquid chromatography with validation, International Journal of Pharmaceutical Chemistry, 04 (02)(2014) 57-61.

[43]. Kumar, Sanjay, and D. R. Harish Kumar. "Importance of RP-HPLC in Analytical Method Development: A Review." International Journal of Pharmaceutical Sciences and Research (IJPSR), vol. 3, no. 12, 2012, pp. 4626-4633. ISSN: 0975-8232.

[44]. N.Thyagarajapuram ,KS Alexander. A SIMPLIFIED METHOD FOR THE ESTIMATION OF AMIODARONE HYDROCHLORIDE BY REVERSE-PHASE HIGHPERFORMANCE LIQUID CHROMATOGRAPHY. J Liq Chrom & Rel Technol. (2003).26: 1315-1326.DOI: https:// doi.org/10.1081/JLC-120020113.

[45]. Gupta, Suyash, et al. "A Review on Novel Analytical Method Development and Validation by RP-HPLC Method." Indian Journal of Forensic Medicine & Toxicology, vol. 15, no. 4, Oct.-Dec. 2021, pp. 3476-3485.

[46]. K, Sonia, Beddi Bhavya Shree, and K. S. Lakshmi. "HPTLC Method Development and Validation: An Overview." Journal of Pharmaceutical Sciences and Research, vol. 9, no. 5, 2017, pp. 652-657.

[47]. K, Sonia, Beddi Bhavya Shree, and K. S. Lakshmi. "HPTLC Method Development and Validation: An Overview." Journal of Pharmaceutical Sciences and Research, vol. 9, no. 5, 2017, pp. 652-657.

[48]. Chaudhry, Shekhar, and Rajendra B. Patil. "A Review on Stability Indicating Analytical Method Development and Validation by HPTLC." American Journal of PharmTech Research, vol. 8, no. 1, 2018. ISSN: 2249-3387.

[49]. ICH Q2 (R1), Validation of Analytical Procedures: Text and Methodology, Geneva Switzerland, 2003.

[50]. Ravisankar, P., Ch. Lokapavani, Ch. Devadasu, and G. Devala Rao. "HPTLC: A Versatile Method for Rapid Analysis of Pharmaceutical Formulations and Comparison with Other Chromatographic Techniques and Its Applications." Indian Journal of Research in Pharmacy and Biotechnology, pp. 1210-1211. Print ISSN: 2321-5674, Online ISSN: 2320-3471.

[51]. R. B. Patel, A. B. Patel, M. R. Patel, M. B. Shankar and K. K. Bhatt, Anal. Lett., 2009, 42, 1588–1602.

[52]. R. B. Patel, M. R. Patel, M. B. Shankar and K. K. Bhatt, J. AOAC Int., 2009, 92, 1082–1088.

[53]. R. B. Patel, M. B. Shankar, M. R. Patel and K. K. Bhatt, J. AOAC Int., 2008, 91, 750–755 .

[54]. Arima, Hidetoshi, and Alina Pyka**.** "Detection Progress of Selected Drugs in TLC." BioMed Research International, 2014, https://doi.org/10.1155/2014/732078.

[55]. Kaal, Erwin, and Hans-Gerd Janssen. "Extending the molecular application range of gas chromatography." Journal of Chromatography A 1184. 1 2008, pp. 43-60.

[56]. Grob, Robert L., and Eugene F. Barry, eds. Modern practice of gas chromatography. John Wiley & Sons, 2004.

[57]. I.A. Fowlis, Gas Chromatography-Analytical chemistry by open learning, 2nd Ed., John Wiley & Sons, 1995.

[58]. AL-Bukhaiti, Wedad Q., Anwar Noman, Aseela Saeed Qasim, and Ammar AL-Farga. "Gas Chromatography: Principles, Advantages, and Applications in Food Analysis." International Journal of Agriculture Innovations and Research, vol. 6, no. 1, ISSN (Online): 2319-1473.

[59]. ICH, International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use, Topic Q7: Good ALGIN YAPAR et al. Universal Journal of Pharmaceutical Research 2020; 5(1):47-52 Manufacturing Practices for Pharmaceutical Ingredients 2000.

[60]. Beskan, Umut, et al. "An Overview of Analytical Method Validation." Universal Journal of Pharmaceutical Research, vol.

7, no. 4, 2023, pp. 2456-8058. ISSN 2831-5235 (Print), 2456-8058 (Electronic).

[61]. Bhardwaj, Santosh Kumar, et al. "A Review: HPLC Method Development and Validation." International Journal of Analytical and Bioanalytical Chemistry, vol. 3, no. 2, 2013, pp. 76-81. ISSN 2231-5012.

[62]. T. Bhagyasree, N. Injeti, A. Azhakesan, U.M.V. Rao, A review on analytical method development and validation,International Journal of Pharmaceutical Research & Analysis, Vol 4 (8) (2014) 444-448. 17.

[63]. S. Jain, G. Kaur, V. Saini, A Review on Analytical Method Development and Validation, Asian Journal of Biochemical and Pharmaceutical Research , 3 (4) (2014) 128-142

[64]. WHO Expert Committee on Specifications for Pharmaceutical Preparations.WHO technical Report, series no. 863 – 34th report, Annex 6 –GMP: Guidelines on the validation of Manufacturing processes: 4-7.

[65]. ICH Guidelines Q2 (R2) on validation analytical procedure , 31 march 2022

[66]. .c Jain, K., & Bharkatiya, M. (2018). A comprehensive review: Validation of tablet dosage form. The Pharma Innovation Journal, 7(3), 433-438.

[67]. Lavanya, G., Sunil, M., Eswarudu, M. M., Eswaraiah, M. C., Harisudha, K., & Naga Spandana, B. (2013). Analytical method validation: An updated review. International Journal of Pharmaceutical Sciences and Research, 4(4), 1280-1286

[68]. Chavan, Sushila Dagadu, and Deepa Mahendra Desai. "Analytical Method Validation: A Brief Review." WAJRR, vol. 2581-9615, 2023.

[69]. USP (2009) Chromatography System Suitability. United States Pharmacopeial Convention.

[70]. Chan CC, Lam H, Lee YC, Zhang XM (2004) Analytical Method Validation and Instrument Performance Verification, Hoboken, John Wiley & Sons (Wiley Inter science), New Jersey.

[71]. Magnusson, B. and Örnemark, U. EURACHEM Guide: The Fitness for Purpose of Analytical Methods: A Laboratory Guide to Method Validation and Related Topics, issued in 1998.) Available at: https://www.eurachem.org/images/stories/Guides/pdf/MV_guide_2nd_ed_EN.pdf (Accessed March 17, 2015).

[72]. Gowik, P. (2009) The validation of methods for regulatory purposes in the control of residues. J. Chromatogr. A, 1216, 8051–8058.

[73]. Peters, F.T., Drummer, O.H., and Musshoff, F. (2007) Validation of new methods. Forensic Sci. Int., 165, 216–224.

[74]. Grob, K. (2007) Verification of results to improve the quality of analytical data: a proposal. J. Chromatogr. A, 1150,93–99.

[75]. Sabale, S., & Thorat, S. (2021). An overview on validation process in pharmaceutical industries. Scholars Academic Journal of Pharmacy, 10(6), 95-101.

[76]. Kaur, H., Singh, G., & Seth, N. (2013). Pharmaceutical process validation: Review article. Journal of Drug Delivery & Therapeutics, 3(4), 189-194.

[77]. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), & Center for Biologics Evaluation and Research (CBER). (2016). Q7 good manufacturing practice guidance for active pharmaceutical ingredients: Guidance for industry (ICH Revision 1[12.5]). U.S. Food and Drug Administration.

[78]. Lakshmana Prabu, S., Suriyaprakash, T. N. K., Thirumurugan, R., & Shanmugarathinam, A. Process validation: A review. Pharma Times, 2014,46(4).

[79]. Good manufacturing practices guidances on validation WHO Expert Committee on Specifications for Pharmaceutical Preparations Fifty-third report October 2014.

[80]. Kaur, H., Singh, G., & Seth, N. (2013). Pharmaceutical process validation: Review article. Journal of Drug Delivery & Therapeutics, 3(4), 189-194.

[81]. Hyde, John, Andrew Hyde, and Paul Pluta. "FDA's 2011 Process Validation Guidance: A Blueprint for Modern Pharmaceutical Manufacturing." IVT Network, www.ivtnetwork.com.

[82]. Prajapati, Roshani, and Kashif Hussain. "Process Validation of Rabeprazole

Sodium Tablets (Rabi 20).” International Journal of Research in Engineering, Science and Management, vol. 2, no. 12, Dec. 2019.

[83]. Tandel, Jignakumari Manubhai, Zarna R. Dedania, and K. R. Vadalia. “Review on Process Validation of Pyrazinamide Tablets.” International Journal of Advances in Pharmaceutical and Biological Chemistry (IJAPBC), vol. 1, no. 3, July-Sept. 2012, ISSN: 2277-4688.

[84]. Jyakhwa, Ureena, Deepika Joshi, Praveen Kumar Ashok, and Neera Chikanbanjar. “Concurrent Process Validation of the Salbutamol Tablet IP.” Pharmacy Practice and Research, vol. 1, no. 1, 2020, pp. 82–93.

[85]. Sharma, Sumeet, and Gurpreet Singh. “Process Validation in Pharmaceutical Industry: An Overview.” Journal of Drug Delivery & Therapeutics, vol. 3, no. 4, 2013, pp. 184–188.

[86]. Verma, V., Nautiyal, U., Senthil Kumar, M., & Kant, C. (2014). Process validation of tablets: An overview. Asian Pacific Journal of Health Sciences, 1(1), 31-38.

[87]. Singh, S., Hussain, K., & Ashok, P. K. (2022). Process validation approach for pharmaceutical formulation: An updated review. International Journal of Research and Analytical Reviews, 9(3), 891.

[88]. Singh, Sony, Kashif Hussain, and Praveen Kumar Ashok. “Process Validation of Celecoxib 200 mg Capsules.” IJRAR, vol. 9, no. 3, Aug. 2022, pp. 1-10.

[89]. Nieves, R., & Reyes, L. B. (2024). Process validation: A study on batch size increase in downstream processes. Manufacturing competitiveness PRCR 2023 http://hdl.handle.net/20.500.12475/2003

[90]. Jain, K., Agarwal, P., & Bharkatiya, M. (2018). A review on pharmaceutical validation and its implications. International Journal of Pharmacy and Biological Sciences, 8(2), 117-126.

[91]. Wadher, Dr. S. J., Sachin Tayde, and Dr. S. G. Gattani. “Validation: A Review.” World Journal of Pharmaceutical Research, vol. 6, no. 8, 2017, pp. 2228-2241.

[92]. Singh, S., Hussain, K., and P. K. Ashok. “Process Validation Approach for Pharmaceutical Formulation: An Updated Review.” International Journal of Research and Analytical Reviews (IJRAR), vol. 9, no. 3, 2022, pp. 203-215.

[93]. Patil, Satyajit Samapatrao, and Dr. K.A. Wadkar. "Pharmaceutical Process Validation: A Review." International Journal of Research Publication and Reviews, vol. 3, no. 12, Dec. 2022, pp. 360-364.

[94]. Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-operation Scheme. Guide to Good Manufacturing Practices for Medicinal Products: Annexes (PE 000-15). May 2021.

[95]. Nikam, Umed A., et al. “An Overview of Pharmaceutical Process Validation of Solid Dosage Form.” Current Pharma Research, vol. 3, no. 2, 2013, pp. 824-835.

[96]. Kakad, Sudarshan Balasaheb, Mahesh Hari Kolhe, and Tushar Pradip Dukre. “A Review on Pharmaceutical Validation.” IJPQA, vol. 11, no. 3, July 2020–Sept. 2020.

[97]. Waghmare, Sumesh B., Sidheshwar S. Patil, Raviraj R. More, Rahul S. Solunke, Sharad V. Usnale, and Vidya S. Jadhav. “A Brief Review on Pharmaceutical Validation and Pharmaceutical Process Validation.” World Journal of Pharmaceutical Research, vol. 11, no. 17, 2022, pp. 276-287.

[98]. Kathiresan, K., C. Moorthi, Y. Prathyusha, Bharath Reddy Gade, M. Bhagath Kumar Reddy, and R. Manavalan. “An Overview of Pharmaceutical Validation.” RJPBCS, vol. 1, no. 4, Oct.–Dec. 2010, pp. 1031-1032.

[99]. Reddy, Manasa S., and Chandramouli R. “Functional Overview of Process Validation of Tablets – A Critical Review.” Journal of Pharmaceutical Research, vol. 16, no. 3, Jul.-Sept. 2017, pp. 268-276.

[100]. Yadav, Chandni, Vaishnav, Rajat, and Goyal, Anju. “Ijppr.Human.” Ijppr.Human, vol. 14, no. 1, 2018, pp. 55-66.

[101]. Kandharkar, Kaustubh, Sakhare, Mayur, and Akmar, Nikhil. “Review on Industrial Process Validation of Tablet Dosage Form.” International Journal of Interdisciplinary and Multidisciplinary Studies (IJIMS), vol. 1, no. 4, 2014, pp. 112-124.

[102]. World Health Organization. Good Manufacturing Practices for Pharmaceutical Products: Annex Guidelines on the Validation of Manufacturing Processes, WHO/Pharm/93-562, rev. 3, pp. 5.
[103]. Jindal, Diksha, Hardeep Kaur, Rajesh Kumari Patil, and Hanumanthrao Chadershekar Patil. "Validation – In Pharmaceutical Industry: Equipment Validation: A Brief Review." Adesh University Journal of Medical Sciences & Research, vol. 2, no. 2, July–Dec. 2020, pp. 94-97.
[104]. Karthick, C., and K. Kathiresan. "Pharmaceutical Process Validation: A Review." Journal of Drug Delivery & Therapeutics, vol. 12, no. 1-s, 2022, pp. 164-170.
[105]. Daksh, Shashi, and Anju Goyal. "Analytical Method Development and Validation: A Review." Chemistry Research Journal, vol. 5, no. 3, 2020, pp. 173–186.
[106]. Soumia Belouafa, Statistical tools and approaches to validate analytical methods: methodology and practical examples, International Journal of Metrology and Quality Engineering, 2017, 8(9); 1-10.
[107]. Bhavesh Vaghela, et al., Development and validation of dissolution procedures, Journal of Applied Pharmaceutical Science 01 (03); 2011: 50-56.
[108]. Douglas Chesher, Evaluating Assay Precision, Clin Biochem Rev, 2008; 29 (Suppl 1): S23–S26.
[109]. Mohammad T et al., HPLC Method Development and Pharmaceutical Validation Analysis- A for Review. Internationale Pharmaceutica Sciencia. 2012, 2(3), 14
[110]. Vibha G et al., Development and validation of HPLC method - a review. International Research Journal of Pharmaceutical and Applied Sciences. 2012, 2(4), 22-23.
[111]. Pawar PV et al., Development and validation of UV-HPLC method on tablet dosage form: a review. International Journal of Pharma Research and Development. 2011, 3(1), 187.
[112]. Validation of Analytical Methodology.ICH-Guidelines 1996, 11. Procedures: Q2B,Geneva. (CPMP/ICH/281/95).
[113]. Ghulam A. Shabir, Step-by-Step Analytical Methods Validation and Protocol in the Quality System Compliance Industry, Institute of Validation Technology, 4-13.
[114]. https://machan11.tripod.com/System%20Suitability.htm
[115]. Singh, Prabh Simran, and Gagan Shah. "Analytical Method Development and Validation." Journal of Pharmacy Research, vol. 4, no. 7, 2011, pp. 2330–2332.