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METHOD DEVELOPMENT, VALIDATION AND STRESS DEGRADATION STUDIES OF BULK DRUG AND ITS PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

An essential step in the drug discovery process is the development of analytical methods and subsequent technique validation. Despite the drug's good potency, the lack of a recognised analytical method prevents the drug from being sold. This is to guarantee the standard and the drug's safety. The main goal of this review is to provide information on the traditional and cutting-edge methods used to analyse drugs in both their unprocessed and processed forms, as well as to examine the stability of the drugs in the presence of excipients and other stressors that may occur during the course of their shelf life. The review paper sheds light on hyphenated techniques such LC-MS-MS, LC-NMR-MS, GC-MS, and LC -MS for the analysis and impurity profiling of medicines. The development of bioanalytical methods for the quantitative detection of pharmaceuticals in various biological matrices is also covered in this review. Additionally, it offers a way to assess the medications' biological safety via addressing the SIAMs (stability indicating assay methods).

Keyword: Validation, Stability indicating, Impurity, bioanalytical, HPLC, HPTLC.

I. INTRODUCTION

Analytical chemistry is a branch of chemistry which deals with identification of components (qualitative) and determination of quantity of components (quantitative) of substances or samples or mixture. There are two types of analysis, one is qualitative analysis and another one is quantitative analysis. In qualitative analysis, there is identification of components or analyte of mixture or sample is carried out. In quantitative analysis, there is determination of amount of components or analyte of mixture or sample is carried out.(1) Analytical data is required not only in chemistry but also in other sciences like biology, zoology, arts such as painting and sculpture, archaeology, space exploration and clinical diagnosis. Important areas of application of analytical chemistry are quality control in manufacturing industries, monitoring and control of pollutants, clinical and biological studies, geological assays, fundamental and applied research.(2)

1. ANALYTICAL METHOD

Analytical method includes use of a specified technique and detailed-stepwise instructions which are used in qualitative, quantitative or structural analysis of a sample for one or more analytes.(2) Analytical methods are mainly classified into two types: Classical methods and Instrumental methods (Figure 1). A method in which the signal is proportional to the absolute amount of analyte is called classical method. A method in which the signal is proportional to the analytes concentration is called instrumental method.(3)

Classical methods are divided into 3 main types are:

a) Separation of analyte, b) Qualitative analysis and c) Quantitative analysis.

Separation of analyte includes extraction, distillation, precipitation and filtration. Qualitative analysis includes boiling point, freezing point, colour, odour, density, reactivity and refractive index. Quantitative analysis includes gravimetric analysis and volumetric analysis.

Instrumental methods are divided into four main types are:

a) spectroscopic methods, b) electrochemical methods, c) chromatographic methods and d) other techniques.

Spectroscopic methods include ultraviolet-visible spectroscopy, infrared spectroscopy, Raman spectroscopy, atomic absorption spectroscopy and atomic emission spectroscopy, x-ray spectroscopy and nuclear magnetic spectroscopy. Electrochemical methods include Potentiometry, Coulometry and Voltametry. Chromatographic methods include column chromatography, paper chromatography, thin layer chromatography, high performance liquid chromatography, gas chromatography and modern methods (LC-MS, GC-MS, LC-MS-MS, GC-MS-MS, LC-NMR and GC-NMR). Other techniques include x-ray methods, radioactivity, mass spectrometry, optical methods (Refractometer, optical rotation) and thermal methods (Thermogravimetry, differential thermal analysis and differential scanning calorimetry).(4)

2. INTRODUCTION TO SPECTROSCOPY

Spectroscopy is the study of interaction of electromagnetic radiation with matter. These interactions involve absorption and emission of radiation (energy) by the matter. Spectroscopy are of two types, absorption spectroscopy and emission spectroscopy. The study of electromagnetic radiation absorbed by the sample, in the form of spectra is called absorption spectroscopy (UV-visible, IR, NMR, microwave and Radiowave spectroscopy). The study of electromagnetic radiation emitted by the sample, in the form of spectra is called

emission spectroscopy (flame photometry and fluorimetry). Spectroscopy is useful for the study of atomic and molecular structure and used in the analysis of a wide range of samples. Atomic spectroscopy is the study of interaction of electromagnetic radiation with atoms, changes in energy takes place at atomic level (e.g. atomic absorption spectroscopy and flame photometry). Molecular spectroscopy is the study of interaction of electromagnetic radiation with molecules, changes in energy takes place at molecular level (e.g. ultraviolet and infrared spectroscopy).[6]

2.1 UV-Vis spectroscopy

In UV-visible spectroscopy, the amount of light absorbed at each wavelength of UV and visible region of electromagnetic spectrum is measured. This absorption spectroscopy uses electromagnetic radiations between 200 nm to 800 nm and is divided into the ultraviolet (UV, 200-400 nm) and visible (VIS, 400-800 nm) regions[7]

The principle of UV-Visible spectroscopy is based on the absorption of ultraviolet light or visible light by sample or chemical substance which results in the production of different spectra. When a molecule absorbs UV radiation, the electron present in that molecule undergo excitation, this causes transition of electron within a molecule from a lower level to a higher electronic energy level and the ultraviolet emission spectra arise from the reverse type of transition. Most commonly used solvents in UV spectroscopy are water, methanol, ethanol, ether, chloroform, carbon tetrachloride, cyclohexane and dichloroethane. Applications of UV spectroscopy are detection of functional groups, detection of conjugation, detection of geometrical isomers and detection of impurities,detection of functional groups, detection of conjugation, detection of geometrical isomers and detection of impurities.[6]

2.2 Instrumentation of UV-Visible spectroscopy

A. Radiation sources:

Most commonly used radiation sources are tungstan lamp, hydrogen discharge lamp, deuterium lamp, xenon discharge lamp and mercury arc.

B. Wavelength selector:

The monochromator is used to disperse the radiation according to the wavelength. The basic elements of a monochromator are an entrance slit, a dispersing element and an exit slit.

C. Sample cell: In UV-Visible spectroscopy sample containers are used to hold liquid sample are called as cells or cuvettes. Cuvettes are made from quartz.

D. Photo detector: Most commonly used detectors in UV spectrophotometer are barrier layer cell, photocell and photomultiplier tube.

E. Readout device: The output from the detector is suitably amplified and then displayed on a readout device.[6]

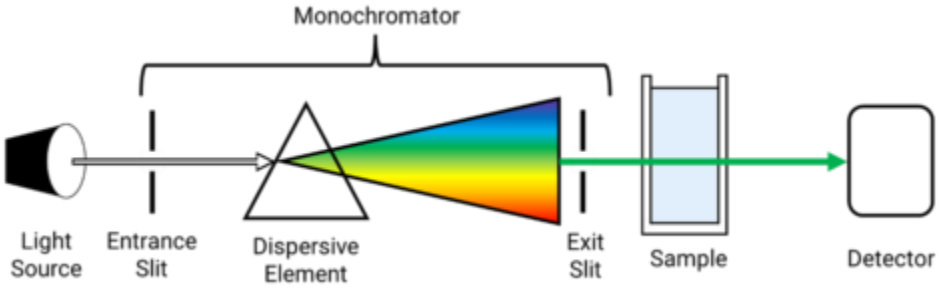

Fig 1: Instrumentation of UV-Visible spectroscopy

3. INTRODUCTION TO CHROMATOGRAPHY

Chromatography is a physicochemical method for separation of mixture of compounds. Chromatography is a method of separation of mixture of compounds into individual components between two phases, a stationary phase and a mobile phase[8]. Chromatography is classified as follows:

1. Based on interaction of solute to stationary phase

- Adsorption chromatography
- Partition chromatography
- Ion exchange chromatography
- Molecular exclusion chromatography

2. Based on chromatographic bed shape

- Column chromatography
- Planar chromatography
- Paper chromatography
- Thin layer chromatography
- Displacement chromatography

3. Techniques by physical state of mobile phase

- Gas chromatography
- Liquid chromatography
- Affinity chromatography

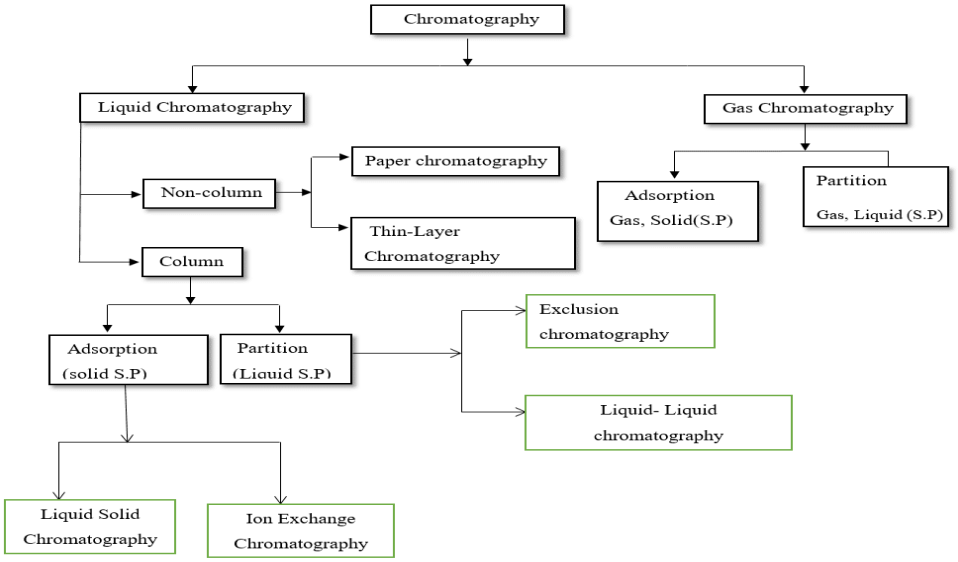

Fig 2: Types of Chromatography

3.1 HPLC

HPLC stands for high performance liquid chromatography or high-pressure liquid chromatography. HPLC can separate, identify and quantify the compounds present in any sample which can be dissolved in liquid[(9)]. The main principle of liquid chromatography is adsorption. It is a chromatographic technique in which mobile phase is liquid. Sample is in the form of liquid solution. Sample is injected into a column of a porous material (stationary phase) and a liquid phase (mobile phase). Sample move through the column with mobile phase by high pressure delivered by a pump. Sample components travel according to their affinity towards the stationary phase. The component which has more affinity towards the stationary phase travels slower. The component which has less affinity towards the stationary phase travels faster. The components are separated from each other.[(10)] The most common solvents used for HPLC are n-hexane, methylene chloride, chloroform, methyl-t-butyl ether, Tetrahydrofuran (THF), Isopropanol (IPA), Acetonitrile (MeCN or CAN), Methanol (MeOH) and water.[(11)] Fundamental chromatographic parameters are efficiency (number of theoretical plates), retention factor, selectivity, resolution and pressure. Applications of HPLC are chemical separation, purification and identification. Other applications of HPLC include pharmaceutical applications, environmental applications, forensics, clinical, food and flavor.[(12)]

3.2 Instrumentation of HPLC

Components of the HPLC system:

A. Solvent reservoir, mixing system and degassing system

B. High pressure pump

C. Sample injector

D. Column

E. Detector

F. Data recording system

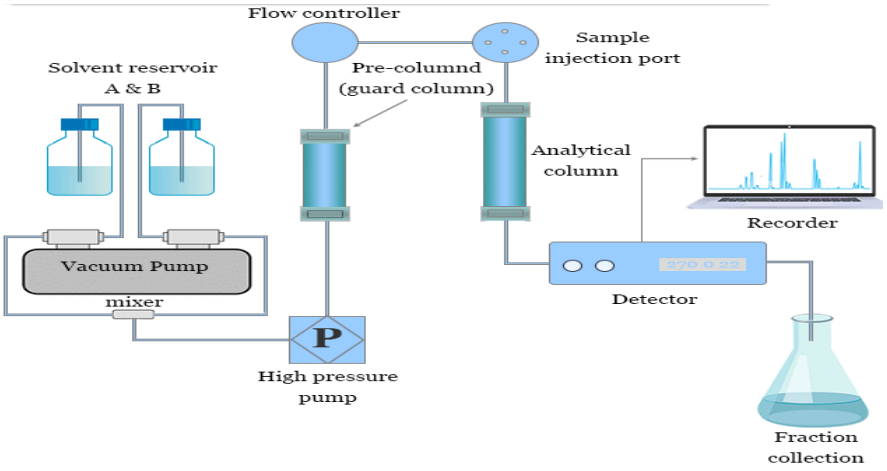

Fig 3: Instrumentation of HPLC

1. Solvent reservoir, mixing system and degassing system:

Solvent reservoir stores the solvent (mobile phase). These are glass or stainless-steel containers. The most common type of solvent reservoir is glass bottle.[13] In addition to delivery of mobile phase, the pump must mix solvents with high accuracy and high precision. Two types of mixing unit are low pressure mixing and high pressure mixing[14]. Degassing system removes entrapped air bubbles from the solvent. Degassing is done by degasser techniques are ultra-sonication and filtration [13].

2. High pressure pump:

The role of pump is to force a liquid and give a specific flow rate. Flow rate is expressed in millilitres per minute (ml/min). Normal flow rate is 1-2 ml/min. Pump pressure range is 6000-9000 psi (400-600 bar)[9]. Commonly used pump types are constant pressure pump, syringe type pump and reciprocating piston pump [15].

3. Sample injector:

The liquid sample is introduced into the mobile phase by sample injector. Sample valve come between the pump and the column[13]. An injector (auto sampler) is able to inject the sample into the continuous flowing mobile phase stream that carries the sample into the HPLC column. Typical sample volumes are 5-20 microliters (µl)[9]. Two types of injector are manual injector and automatic injector.[15]

4. Column:

Column is a place where actual separation of components takes place. Column is made up of stainless steel. It is 5-25 cm long and 2-4.6 cm internal diameter.[9]

5. Detector:

The detector can detect the individual component that elute from the column and convert the data into an electrical signal (Chawla G and Chaudhary KK, 2019). Types of detector used are of two types, specific detectors and bulk property detectors. Specific detectors include UV-VIS detector, photo diode array detector, fluorescence detector and mass spectrometric detector. Bulk property detectors include refractive index detector, electrochemical detector and light scattering detector.[15]

6. Data recording system: The output is recorded as a series of peaks and the area under the peak can be calculated automatically by the computer linked to the display.[12]

4. ANALYTICAL METHOD DEVELOPMENT

Analytical method development is the activity of selecting an accurate assay procedure to find out the composition of a formulation. Development of analytical method is the process which is used to prove that an analytical method is suitable for use in laboratory. Analytical methods must be used inside GMP and GLP environments and should be developed by using the given protocols and acceptance criteria in the ICH guidelines Q2 (R1)[16]

The requirements for method development are as follows:

1) Qualified analysts

2) Instruments-qualified and calibrated

3) Documented methods

4) Reliable reference standards

5) Sample selection and integrity

6) Change control[16]

Analytical method development is useful for:

1) New process and reactions

2) New molecule development

3) Active ingredients (Macro analysis)

4) Residues (Micro analysis)

5) Impurity profiling

6) Degradation studies

7) Herbal products[16]

4.1 Steps involved in method development

1) Standard analyte characterization:

• All the known information about analyte and its structure is collected for example physical and chemical properties.

• The standard analyte with 100% purity is received. Proper storage condition is arranged such as freezer, refrigerator and desiccators.

• Estimation of multiple components from the sample matrix are analyzed, the number of components are considered, data is compiled and the availability of standards is determined for each component.

• Those methods (Spectroscopic, HPLC, GC, MS, etc.) are considered only, which are suitable with sample stability.[17]

2) Method requirements:

Requirement of analytical methodology is necessary to establish the analytical figures of advantage such as linearity, precision, accuracy, Limit of Detection, Limit Of Quantification, specificity, selectivity and range etc. are marked. [17]

3) Literature survey and prior methodology:

All types of information (Physical properties, chemical properties, solubility, manufacturing, related analytical methods etc.) regarding the analyte are obtained by doing literature survey by referencing books, journals, pharmacopoeias etc. Chemical Abstract Service (CAS) automated computerized literature searches are also helpful for literature survey.[17]

4) Selecting a method:

The methodology is developed by using the information obtained from the literature. The method is being revised where necessary. Few times, there is a need to include extra instrumentation to reproduce, modify, validate or improve available methods for samples and analytes. If there is no any established method for analyte in the literature, then such compounds are searched which are identical in chemical properties and structure of analyte.[17]

5) Proper instrumental arrangement and initial studies:

The necessary equipment must be set up. Installation Qualification (IQ), Operational Qualification (OQ) and Performance Qualification (PQ) are verified by using Standard Operating Procedures (SOP's). Every time new things (e.g. solvents, filters and gases) are used. For example, method development is never initiated with previously used HPLC column. The analyte solution, standard solutions of known concentrations and solvents are prepared. It is necessary to begin with a genuine, known standard instead a complex sample matrix. If the sample is very close to the standard (active drug), after that it is probable to begin work with the actual sample [17].

6) Optimization:

A single parameter during optimization is changed at a time and the set of terms is different, instead of using a trial and error approach. There is work has been done from the systematic plan and each case is documented in a lab notebook.[17]

7) Proper documentation of analytical figures of merits:

The initially determined analytical figures of merit are Limit Of Detection (LOD), Limit Of Quantification (LOQ), linearity, evaluation time, expenses, sample preparation etc. are documented.[17]

8) Evaluation of method development along with actual samples:

The prepared solution for analyte needs to be specific, absolute identification of the peak interest of the medicament apart from all the different matrix parts.[17]

9) Determination of percentage recovery of actual sample and demonstration of quantitative sample analysis:

The percent recovery of spiked, genuine standard analyte into a sample matrix that do not have analyte is estimated. Ability to reproduce recovery from sample to sample has been optimized. If the results are reproducible then it is not required to obtain 100% recovery. The verification of validity of analytical method is done only by laboratory study. Therefore, documentation of such successful studies is a basic requirement to determine a method is satisfactory for its desired application.[17]

5. VALIDATION

Validation is a concept developed in the United States in 1978. The concept of validation has been broaden over the years to achieve many activities like from analytical methods used to control quality of drug substances and drug products up to computerized systems for clinical trials, process control or labelling. Validation is best seen as a necessary and prime part of cGMP.

The word validation means evaluation of validity or the act of proving effectiveness. Validation is a team work involving people from different branches of plants. Method validation is a "process of establishing documented evidence" that provides a high level of guarantee that the product (equipment) will meet the requirements of the desired analytical applications.[18]

5.1 Importance of validation

• Assurance of quality

• Minimal batch failure

• Reduction in rejections

• Improved efficiency and productivity

• Increased output

• Reduced testing in process and in finished goods[18].

5.2 Types of validation

There are four types of validation:

1) Equipment validation

a. Design Qualification

b. Installation Qualification

c. Operational Qualification

d. Performance Qualification

2) Process validation

a. Prospective validation

b. Retrospective validation

c. Concurrent validation

d. Revalidation

3) Analytical method validation

4) Cleaning validation.[18]

Types of analytical procedures to be validated

• Identification tests

• Quantitative tests for impurities content

• Limit tests for the control of impurities

• Quantitative tests of the active moiety in samples of drug.[18]

5.3 Steps in method validation

1) Develop a validation protocol, an operating procedure or a validation master plan for the validation.

2) Define the scope, purpose and applications of the method.

3) Define the performance parameters and its acceptance criteria.

4) Define validation experiments.

5) Verify related performance characteristics of equipment.

6) Qualify materials, ex. Standards and reagent.

7) Perform pre-validation experiments.

8) Adjust method parameters or/and acceptance criteria if required.

9) Perform full internal (and external) validation experiments.

10) Develop SOPs for implementing the method in the routine.

11) Define criteria for revalidation.

12) Define type and frequency of system suitability tests and/or Analytical Quality Control (AQC) checks for the routine.

13) Document validation experiments and results in the validation.[18]

5.4 Parameters (components) of method validation

1) Accuracy

2) Precision

3) Linearity

4) Limit of detection

5) Limit of quantitation

6) Specificity

7) Range

8) Robustness

1) Accuracy:

Accuracy is defined as the closeness of the test results to the true value.

2) Precision:

Precision is defined as the measurement of closeness of agreement for multiple measurements on the same sample. The precision is expressed as the relative standard deviation. %RSD = Standard deviation/Mean ×100

3) Linearity:

Linearity is the ability of analytical procedure to obtain a response that is directly proportional to concentration (amount) of analyte in the sample. Linearity is expressed as the confidence limit around the slope of the regression line.

4) Limit Of Detection (LOD):

LOD is defined as lowest amount (concentration) of analyte in a sample that can be detected or identified, not quantified. LOD is expressed as a concentration at a specified signal: noise ratio, usually 3:1.

LOD = 3.3 × S/ SD

5) Limit Of Quantitation (LOQ):

LOQ is defined as lowest amount (concentration) of analyte is a sample that can be quantified. For LOQ, ICH has recommended a signal: noise ratio 10:1.

LOQ = 10 × S/SD

6) Specificity: Specificity is defined as the ability of an analytical method to measure the analyte clearly in the presence of other components. This definition has following implications:

a. Identification

b. Purity tests

c. Assay

7) Range: The range of the method is the interval between upper level and lower level of analyte that have been determined with acceptable accuracy, precision and linearity. It is determined on either a linear or nonlinear response curve and expressed in the same unit as the test results are expressed.

8) Robustness: Robustness is defined as the measurement of capacity of analytical procedure to remain unaffected by small variations in method parameters.[10]

6. STRESS DEGRADATION STUDIES

It's a method of subjecting the drug substance or drug product to stress with varied strengths of stressing agents to obtain the degradation. The stressed samples were analyzed using an LC system equipped with a PDA detector and monitored for the separation of degradation products formed under the stressed conditions and the peak purity of the analyte peak. The method is considered as stability-indicating for the estimation of the drug if it meets the peak purity requirement.[19,20]

Forced degradation studies are conducted basically to meet the following objectives:

• To investigate the likely degradation products; this, in turn, helps to establish the degradation pathways and the intrinsic stability of the drug molecule.

• To provide a foundation for developing a suitable stability-indicating method.

• Ensure the force degradation limit of 2–20%. The major forced degradation studies which are to be carried out are as follows:

a. Thermolytic degradation

This stress testing method studies the degradation that is caused by exposure to temperature high enough to induce bond breakage. Solid-state reactions often proceed in an autocatalytic pathway involving an induction period (lag), followed by a period of rapidly increasing degradation and then slowing down of the degradation rate as the compound is consumed. Thus, solid-state reaction kinetics will often follow an S-shaped curve when degradation vs. time is plotted. Thus, before conducting thermolytic degradation, determine the melting point of the compounds of interest. Then, choose a temperature of 70°C for all the drugs for which melting point is 150°C, stress the samples at 105°C. Keep the samples directly exposed in the oven for 1 week or until about 2–20% degradation is achieved, whichever is earlier. Stress the drug substance, placebo, and drug product separately. In the case of the multicomponent drug products, stress testing of placebo with other actives excluding the one at a time shall be performed additionally.

b. Hydrolytic degradation

Drug degradation that involves hydrolysis reaction is called hydrolytic degradation. Hydrolysis reactions are typically acid or base catalyzed. Acidic, neutral, and basic conditions should therefore be employed in order to induce potential hydrolytic reactions. As these hydrolytic stress studies are to be conducted in aqueous solutions, solubility of the drug molecule of interest in water has to be estimated first. Many small molecule drugs are not soluble in water at the concentrations typically used for analytical evaluations (0.1 to 1 mg/mL); in those cases either a slurry or suspension must be used to examine the hydrolytic stability of a compound, or a cosolvent must be added to facilitate the dissolution under the conditions of low solubility. Two most commonly used cosolvents are acetonitrile and methanol. Methanol has the potential of participating in the degradation chemistry which has to be used with caution especially under acidic conditions when the compound being tested contains a carboxylic acid, ester, or amide.

Acetonitrile is generally regarded as inert solvent and is typically preferable to methanol in hydrolytic stress testing studies. However, acetonitrile is not completely inert and can participate in the degradation reactions, leading to art factual degradation results.

The other cosolvents that are recommended for the hydrolytic stress testing studies are shown below.

Table 1: Cosolvents that are recommended for hydrolytic stress testing studies

Acidic pH	Neutral pH	Basic pH
Acetonitrile	Acetonitrile	Acetonitrile
DMSO	N-methyl pyrrolidine	DMSO
Acetic acid		Diglyme
Propionic acid		p-Dioxane

The hydrolytic degradations (using water/0.1 M HCl/0.1 M NaOH with or without cosolvent) are recommended to be performed at a temperature of about 70°C with a reflux condenser installed to avoid the loss of evaporation. Reflux until about 2–20% degradation is achieved. Stress the drug substance, placebo, and drug product separately. Neutralize the stressed solutions before injection. Prepare a stressed solution at a higher concentration than that of test concentration. In the case of the multicomponent drug products, stress testing of placebo with other actives excluding the one at a time shall be performed additionally.

c. Humidity stress

Stress the samples to 90% humidity for 1 week. Stress the drug substance, placebo, and drug product separately. In the case of the multicomponent drug products, stress testing of placebo with other actives excluding the one at a time shall be performed additionally.

d. Oxidative degradation

Oxidative degradation is one of the most common mechanisms of drug degradation. Oxidative drug degradation reactions are typically autoxidative, that is, the reaction is radical initiated. Radical initiated reactions start with an initiation phase involving the formation of radicals followed by propagation phase and eventually a termination phase. Thus, the reaction kinetics will often follow S-shaped curve when the degradation vs. time is plotted and will not follow Arrhenius kinetics.

In oxidative stress study, the use of temperature > 30°C is not recommended because the reaction rate in solution may reduce at higher temp due to the decrease in oxygen content of the solvent. Thus, it is always

suggested to perform the degradation with 3% hydrogen peroxide at room temperature (25–30°C) with constant stirring in the dark. Stress for 24 hours or until about 1–20% degradation is achieved or whichever is earlier. Stress the drug substance, placebo, and drug product separately. In the case of the multicomponent drug products, stress testing of placebo with other actives excluding the one at a time shall be performed additionally.

e. Photolytic degradation

Photolytic degradation is the degradation that results from exposure to UV or visible light. Expose the samples to 3 times to 1.2 million lux-hr visible and 200 W-hr/m2 UVA. Stress the drug substance, placebo, and drug product separately. In the case of the multicomponent drug products, stress testing of placebo with other actives excluding the one at a time shall be performed additionally.

Evaluation of stress testing:

Peak purity can be evaluated for the main peak and the major degradants which have the peak heights less than 1 AU. Identify the degradation products by co injection, in case of known impurities and have comparable spectra.

If any known impurity is observed to be increased in stress, it can be examined properly. If process impurity is found to be increased in stress study, it needs to be assessed whether there is any secondary pathway of formation of this impurity via some other degradant route.

After conducting these studies, verify the chromatograms, and observe any peaks merging with respect to main peak and any critical pairs. If any situations were arrived, adjust the mobile-phase compositions, column parameters, etc. and conclude the method parameters.

After method finalization, check the method using different detectors (RI/ ELSD/CE/LC–MS), and compare the data with other detectors like UV, fluorescence, etc. The UV inactive components can be found with these experiments. Identify the mass of major degradant which may be formed greater than 1.0% in stress studies, and try to establish the structures.[21,22]

Table 2: Selected reports of stability indicating methods where no stress testing has been done

Separations	Drugs	Methodology
Separations from process impurities	Benazepril HCL	HPLC
Separations from known / potential degradation products	Canrenone Phenylbutazone Homatropine Methylbromide Felodipine	HPLC HPLC UV- spectrophotometry SFC
Separations from known / potential degradation products and process impurities	Benzodiazepine Piroxicam Fenclorac Azathioprine	HPLC HPTLC GLC CE

Table 3: Selected reports of 'Stability-Indicating' methods where only one stress condition have been employed

Stress conditions	Drugs	Methodology
Acid	Dyclonine HLC Lisinopril	HPLC UV spectrophotometry
Alkali	Allantoin Benzapril Carbachol	HPLC UV IR
Neutral	Physostigmine salicylate	HPLC
Oxidation	Nortriptyline HCL Atenolol	UV HPLC
Light	Nifedipine Ranitidine HCL	HPTLC Spectrodensitometric TLC

Table 4: Selected reports of 'stability indicating' methods where five (and additional) stress conditions have been employed

Stress conditions	Drugs	Methodology
Acid, alkali, oxidation, dry heat, light	Elanapril maleate	HPLC
Acid, alkali, oxidation, dry heat, light (separation from synthetic impurities also seen)	Sildenafil citrate	HPLC
Acid, neutral, alkali, oxidation, light	Nicardipine HCL	HPLC
Acid, alkali, oxidation, dry heat, wet heat, light dry, light wet	Paroxetine	HPLC
Acid, alkali, oxidation, dry heat, light, reduction	Cyproterone acetate	HPLC
Acid, alkali, oxidation, dry heat, light, moisture, sonication	Buspirone HCL	HPLC

DISCUSSION AND CONCLUSION

This article discusses how to develop a method, what validation is, the importance of validation, the different types of validation, how to perform the validation process, and its parameters to demonstrate that the method is suitable for its intended use. The primary goals of analytical method development are identification, purification, and, eventually, validation, to qualify any required drug, etc. Analytical method development aids in understanding critical process parameters and reducing their effects on precision and accuracy. Validation is a technique used in the pharmaceutical industry to ensure that quality work is done in the process that supports the development of medicines and products.

REFERENCES

1. Kenkel J. Analytical Chemistry for Technicians. Lewis Publishers. 2003.

2. Kissinger PT. Instant Notes: Analytical Chemistry. Clin Chem. 2002; 48(12): 2303.

3. Harvey D. Modern analytical chemistry. McGraw-Hill. 2000.

4. Ravisankar P, Navya CN, Pravallika D, Sri DN. A review on stepby-step analytical method validation. IOSR J Pharm. 2015; 5(10): 7-19.

5. Jeffery GH. Textbook of quantitative chemical analysis. Longman. 1989.

6. Chatwal GR, Anand SK. Instrumental Methods of Chemical Analysis. Himalaya Publishing House. 2002.

7. Kumar S. Spectroscopy of organic compounds. Cosmic rays. 2006; 10: 4.

8. Luxminarayan L, Sharma N, Viswas A, Khinchi MP. A review on chromatography techniques. Asian Journal of Pharmaceutical Research and Development. 2017; 1-8.

9. Chawla G, Chaudhary KK. A review of HPLC technique covering its pharmaceutical, environmental, forensic, clinical and other applications. Int J Pharm Chem Anal. 2019; 6(2): 27-39.

10. Vidushi Y, Meenakshi B. A review on HPLC method development and validation. Res J Life Sci. 2017; 2(6): 178.

11. McPolin O. An introduction to HPLC for pharmaceutical analysis. Lulu. 2009.

12. Malviya R, Bansal V, Pal OP, Sharma PK. High performance liquid chromatography: a short review. J Glob Pharma Technol. 2010; 2(5): 22-26.

13. Jena AK. HPLC: highly accessible instrument in pharmaceutical industry for effective method development. Pharm Anal Acta. 2011; 3.

14. Agilent Technologies. The LC Handbook Guide to LC Columns and Method Development. Agilent Technologies. 2016; 16.

15. Hamilton RJ, Sewell PA. Introduction to high performance liquid chromatography. Springer. 1982; 1-12.

16. Chauhan A, Mittu B, Chauhan P. Analytical method development and validation: a concise review. J Anal Bioanal Tech. 2015; 6(1): 1-5.

17. Ravisankar P, Gowthami S, Rao GD. A review on analytical method development. Indian J Res Pharm Biotech. 2014; 2(3): 1183.

18. Lavanya G, Sunil M, Eswarudu MM, Eswaraiah MC, Harisudha K, Spandana BN. Analytical method validation: An updated review. Int J Pharm Sci Res. 2013; 4(4): 1280.

19. Singh S, Junwal M, Modhe G, Tiwari H, Kurmi M, Parashar N, et al. Forced degradation studies to assess the stability of drugs and products. Trends in Analytical Chemistry. 2013;49:71-88.

20. Jain D, Basniwal PK. Forced degradation and impurity profiling: Recent trends in analytical perspectives. Journal of Pharmaceutical and Biomedical Analysis. 2013;86:11-35.

21. Syed G Musharraf., Urooj Fatima., Rahat sultanan. Stress degradation studies and development of stability indicating –TLC densitometry method for determination of Predensolone and chloramphenicol in their individual and combined pharmaceutical formulations reversed phase. Chem.Central.J 2012; 6(7): 134 – 137.

22. Nahla Nour El-Din Ahmed Salama., Afaf Osman Mohamed. Stability-Indicating Methods for the Determination of Sertaconazole Nitrate by Micelle-Enhanced Spectrofluorimetry and TLC-Densitometry. Bull. Chem. Soc. Ethiop. 2009; 23(2):167- 174.