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Principles of analytical chemistry to drug analysis &Stability Indicating Assay Method (SIAM)

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ABSTRACT

Pharmaceutical analysis is the integral part of the pharmaceutical sciences. Pharmaceutical analysis is the application of principles of analytical chemistry to drug analysis. The stability of the active component is a major criterion in determining the suitability of the dosage form. The Stability-Indicating Assay Method (SIAM) is a quantitative analytical procedure used to detect a decrease in the amount of the active pharmaceutical ingredient (API) present due to degradation. International Conference on Harmonization (ICH) Guidelines has made mandatory the requirement of SIAM. Stability is defined as the capacity of a drug substance or a drug product to remain within specifications established to ensure its identity, strength, quality, and purity throughout the retest period or expiration dating period. According to ICH, the guidance is provided to design of stability studies for drug substances and drug products that should result in a statistically acceptable level of confidence for the established retest or expiration dating period for the formulation. An elaborate definition of stability-indicating methodology is, however, provided in the United States-Food and Drug Administration (US-FDA) stability guideline of 1987 and the draft guideline of 1998.

Keywords : ICH, Qualitative Analysis, formulation, Stability Indicating

I. INTRODUCTION

Pharmaceutical analysis is the integral part of the pharmaceutical sciences. Pharmaceutical analysis is the application of principles of analytical chemistry to drug analysis. The analytical chemistry may be defined as the science of developing accurate, precise and sensitive methods for determining the composition of materials in terms of elements or compounds which they contain.

In pharmaceutical analysis section, the research analyst is responsible for three important functions:

1) Development of analytical method for raw materials, active ingredients and chemical intermediates of the product.

2) Development of analytical methods for selective analysis of drug in presence of excipients, degradation products and impurities along with identification of degradation products, degradation pathway and

extent of degradation when stored at ambient and accelerated conditions.

3) Development of analytical method for micro and semi micro quantities of drugs and its metabolites in biological system.

Analytical chemistry can be divided into two areas:

- Qualitative Analysis: It deals with the identification and characterization of substances.
- Quantitative Analysis: It provides numerical information concerning the quantity of some species (the analyte) in a measured amount of the sample.

Pharmaceutical analysis is the quantitative measurement of the active ingredient and related compounds in the pharmaceutical product. These determinations require the highest accuracy, precision, and reliability because of the intended use of the data: manufacturing control, stability evaluation, and shelf-life prediction.

Pharmaceutical analysis methods also play an important role to identify and quantify the drug in the formulated product, the rate at which drug is released from its formulation and stability of drug in the formulation. It is used to reveal identify and purity of drug substances and excipients to be used in the preparation of formulation and concentration of specified impurities in the pure drug substance. The key requisite for success in this field is a thorough knowledge of the various fields of chemistry and excellent interactions with the experts of various other disciplines.

The stability of the active component is a major criterion in determining the suitability of the dosage form. Several forms of instability can occur.

- There may be chemical degradation of the drug, leading to substantial lowering of the quantity of the therapeutic agent in the dosage form. This is even of greater significance in the case of drugs with narrow therapeutic indices, where the patient needs to be carefully treated so that serum levels are neither so high that they are potentially toxic, nor so low that they are ineffective.
- Although the degradation of the active drug may not be that extensive, a toxic degradation product may be formed in the decomposition process.
- Instability of a drug product can lead to a decrease in its bioavailability, rather than to loss of drug or the formation of toxic degradation products. This reduction in bioavailability can result in a substantial lowering in the therapeutic efficacy of the dosage form. This can be caused by physical and chemical changes in the excipients in the dosage form, independent of whatever changes the active drug may have undergone.

There may be substantial changes in the physical appearance of the dosage forms.

The prime necessity is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light and to establish a re-test period for the drug substance or a shelf life for the drug product and recommended storage conditions. The Stability-Indicating Assay Method (SIAM) is a quantitative analytical procedure used to detect a decrease in the amount of the active pharmaceutical ingredient (API) present due to degradation. International Conference on Harmonization (ICH) Guidelines has made mandatory the requirement of SIAM. According to FDA guidelines, a SIAM is defined as a validated analytical procedure that accurately and precisely measures active ingredients (drug substance or drug product) free from potential interferences like degradation products, process impurities, excipients, or other potential impurities, and the FDA

recommends that all assay procedures for stability studies be stability indicating.

Stability Indicating Assay Method (SIAM)

Stability is defined as the capacity of a drug substance or a drug product to remain within specifications established to ensure its identity, strength, quality, and purity throughout the retest period or expiration dating period. According to ICH, the guidance is provided to design of stability studies for drug substances and drug products that should result in a statistically acceptable level of confidence for the established retest or expiration dating period for the formulation. An elaborate definition of stability-indicating methodology is, however, provided in the United States-Food and Drug Administration (US-FDA) stability guideline of 1987 and the draft guideline of 1998. Stability-indicating assay methods according to 1987 guideline were defined as the "quantitative analytical methods that are based on the characteristic structural, chemical or biological properties of each active ingredient of a drug product and that will distinguish each active ingredient from its degradation products so that the active ingredient content can be accurately measured". 8 This definition in the draft guideline of 1998 reads as: 'validated quantitative analytical method that can detect the changes with time in the chemical, physical, or microbiological properties of the drug substance and drug product, and that are specific so that the contents of active ingredient, degradation products, and other components of interest can be accurately measured without interference'.

The major changes brought in the new guideline are with respect to:

- Introduction of the requirement of validation, and
- Requirement of analysis of degradation products and other components, apart from the active ingredient(s).

Two terms have been proposed in literature to differentiate the methods that measure quantitatively the component of interest in the sample matrix without separation, and the ones where separation of the drug as well as other degradation product is done.

- Specific SIAM can be defined as "a method that is able to measure unequivocally the drugs in the presence of all the degradation products, excipients and additives, expected to be present in the formulation".
- Selective SIAM can be defined as "a method that is able to measure unequivocally the drugs and all the degradation products in presence of excipients and additives, expected to be present in the formulation"

The development of the selective SIAM is of greater importance as it separates the active component along with all types of degradation products developed through different conditions guided by ICH Q1A [R2].

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