Stability requirements during development of a drug biology essay

Science, Biology

The main theory of stability testing of pharmaceutical drug substances and pharmaceutical dosage forms is to make available information on how the quality and efficiency of a active pharmaceutical ingredient (API) or dosage form varies with time under the influence of a various of environmental conditions like, light, temperature and humidity which intern allow to establish suggested storage conditions, re-testing time and product shelf life. The above said can be monitored qualitatively and quantitatively by developing a stability- Indicating analytical methods (SIAMs). The developed SIAMs can identify the changes over time in the physical and chemical properties of the API and dosage forms [1], so that the components of analyte, degradation impurities and other components of analyte can be precisely estimated without interference. The focus on development of SIAMs for analysis of drugs for medicines is increasing in regulatory viewpoint which can confine impact on product’s marketing approaches.

1. 1. 2 Stability testing of New Drug substances and Drug Products:

The aim of the ICH stability guideline was to illustrate the core stability data package necessary for new drug substances and products in the European Union, Japan and the United States such that the data generated in any of the regions is jointly acceptable in the other two. The guideline applies to the information required for the applications of newchemical entities and drug products [2], but not for abbreviated or abridged applications, clinical trail applications, and so on.

1. 1. 3 Application of Stability indicating analytical methods:

Stability studies are employed to set up the re-testing period of the drug substance and dosage forms that is the span of time it can be stored and administrated without re-analysis before use. The release and shelf life specifications for pharmaceutical dosage forms may differ to put up degradation of analyte or other tolerable changes, which can take place on storage. As ICH drug stability test guideline Q1A (R2), analysis of stability samples should be performed using validated stability indicating analytical method [3-6]. Supplementary guidance is provided only for photo stability testing [7]. Apart from the above, it is required that stress testing on API and dosage forms to provide its intrinsic stability properties to maintain the fittingness of recommended analytical procedure [8-10]. The validated SIAMs will be employed widely for testing the stability samples of both API and pharmaceutical dosage forms.

1. 2 Types of Instrumental Techniques

There are different categories methods for estimation of drugs namely chemical, biological, physical and physicochemical. Out of these, physical and physicochemical are mostly used. Physical properties of substance are investigated by Physical methods. This methodology includes the determination of transparency, solubility, color intensity orspecific gravity, freezing and boiling points, moisture content and melting. Physicochemical methodology includes study of physical phenomenon as an outcome of chemical reactions. Out of the physicochemical methods, optical (polarimetry, emission, refractometry and florescent methods of analysis,

photometry including photocolorimetry and spectrophotometry, nephelometry or turbidimetry), electrochemical (potentiometry, coulometry, polarography, amperometry) and chromatography (thin layer, column, gas-liquid, paper, high performance liquid) methods are generally preferable. Methods involving nuclear reactions such as NMR and paramagnetic resonance (PMR) are now days are most powerful tools. The technique GCMS now powerful tool available. Methods with sophisticated equipment like HPLC, NMR, and Mass Spectroscopy are very costly and create problems of maintenance. Hence these are not preferred by most of the laboratories and small scale industries, which manufacture API and pharmaceutical formulations. However the make use of sophisticated instruments eradicates the difficulties occurs in the estimation of small amounts of impurities and degradation products.

1. 2. 1 Classification of analytical methods

Analytical methods are classified as Classical methods and Instrumental methods

1. 2. 1. 1 Classical methods

Near the beginning of the years, the majority analysis was performed by separating the compounds of attention in a sample by precipitation, extraction or distillation. For qualitative examination, the separated compounds were then treated with reagents that yielded products that could be recognized by their colors, their optical activities or their refractive indexes.

1. 2. 1. 2 Instrumental methods

Early in the twentieth century, researchers began to develop phenomenon different from methods employed for classical methods to resolve analytical problems. The new and highly capable chromatographic and electrophoretic techniques are started to replace extraction, precipitation and distillation to separate compounds from complex mixture prior to their quantitative or qualitative estimation. These newer methods for separation and determination of chemical substances are called as instrumental methods.

1. 2. 2 Types of instrumental methods preferred in the present investigation

The spectrophotometric methodologies involve interaction between analyte and electromagnetic radiation. The atoms there in the analyte are excited by electromagnetic radiation from a selected area of the spectrum and the excited state atoms then releases typical electromagnetic radiation, which are then quantitatively measured by the instrument. Inthis methodology, absorption of electromagnetic radiation is the characteristic possession of the analyte. The term high performance liquid chromatography (HPLC) is used to the column chromatography. In column chromatography mobile phase is a liquid. In HPLC separation, elution of compounds can be completed very rapidly depending on property of the compound such as partition between mobile phase liquids and stationary or adsorption of analyte on stationary phase or ion exchange nature of component or size exclusion. Ultra performance liquid chromatography (UPLC) is a recent technique in liquid chromatography, which enables significant reductions in separation time and solvent consumption. Literature indicates that UPLC

system allows about nine fold decreases in analysis time as compared to the conventional HPLC system using 5µm particle size analytical columns, and about threefold decrease in analysis time in comparison with 3 µm particle size analytical columns without compromise on overall separation [11-15].

1. 2. 3 Importance of HPLC/UPLC in pharmaceutical analysis

HPLC/UPLC gives stead fast quantitative precision and accuracy with a linear dynamic choice adequate to permit for the estimation of the active pharmaceutical ingredients and impurities in the same chromatogram using different kind of detectors, and can be employed on fully computerized instrumentation. HPLC/UPLC gives outstanding reproducibility and is valid to a wide collection of compound types bycareful selection of column chemistry. Separation of chiral species into their individual enantiomers is promising by HPLC. Chiral separation is through pre-column derivatization to yield diasteriomers or adding together the derivatization reagents to the mobile phase to formation of dynamic diasteriomers through the separation process. On the other hand, columns prepared with cellulose based, amylase based or cyclo dextrin or specific chiral moieties as stationary phase can be used.

1. 2. 4 HPLC Instrumentation

The main components of HPLC are: 1. Solvent Reservoir 2. Pump 3. Injection Port 4. Column5. Detector 6. Data Acquisition System

Fig: 1. 2. F1: Schematic diagram of HPLC

1. 2. 4. 1 Solvent Reservoir:

Solvent Reservoirs are used to store Mobile-Phase. Scott Duran bottles are commonly used as solvent reservoirs. The solvent reservoir must be made of inert material such as glass and must be smooth so as to avoid growth of microorganisms on its walls. It can be transparent or can be amber colored. A graduated bottle gives a rough estimate of mobile-phase volume in the bottle. Solvent reservoirs are placed above HPLC system (at higher level) in a tray. They should never be kept directly above the system as any spillage of solvent on the system may damage electronic parts of HPLC.

1. 2. 4. 2 HPLC Pump

The HPLC pump is very important component of the system. The Pump delivers the constant flow of the Mobile Phase or phases so that the separation of the components of the mixture occurs in a reasonable time. There are two types of pumping systems namely Isocratic and Gradient.

1. 2. 4. 3 Injection Port

The sample introduction device such as injector to introduce the sample in a flow of mobile phase at high pressure. It is not possible to use direct syringe injection on column like GC as the inlet pressure in LC is too high. The valve injection through fixed or variable loop is a common way of introducing the sample. The Rheodyne valve is themostly used devise. The loop can be partially or fully filled. There are both the types of injectors available. The advantage of partial filling is the possibility of using small amount of sample,

when there is scarcity of sample. The precision of the injection is 1% RSD and carryover < 1%.

1. 2. 4. 4 HPLC Column

The HPLC Column holds the stationary phase for separating the components of the sample. The columns are usually made up of SS-316 grade steel. Apart from columns, the material of construction of tubing and fittings, plumbing and connections are also very critical. Apart from resistively to corrosion, connections and plumbing should have a very low dead volume.

1. 2. 4. 5 HPLC Detectors

Detect various compounds as they elute out from column. The detector gives response in terms of a milivolt signal that is then processed by the computer integrator to give you a chromatogram. Basically detector consists of a flow-cell through which the mobile phase and resolved sample moves. Optics shine through the detector cell and variation in optical properties are detected. An Ultra violet or UV detector detects absorbance of UV light by chromophores in the analyte compound. A refractive index detector will sense variation in refractive index of mobile phase stream passing through flow-cell as thesample/analyte mixed mobile phase enters the detector. Similarly Fluorescence Detectors checks for Florescence. The Photo Diode Array Detector [DAD] is the most used detector in LC today [16]. The DAD gives a three dimensional view of chromatogram (Intensity Vs Time) and Spectra (Intensity Vs Wavelength) simultaneously. It can be called as Spectro-chromatogram. The detailed analysis of the data reveals more

information on the complexity of co elution and helps in identifying the merged peaks and gives information on peak purity.

Fig: 1. 2. F2: Chromatogram showing the separation of two components seemingly pure