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Review Article

A REVIEW ARTICLE ON INTRODUCTION OF ANALYTICAL INSTRUMENTS ANALYSIS IN PHARMACEUTICAL INDUSTRY ACCORDING TO PHARMACOPOEIA

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ABSTRACT

The development of drugs brought about a revolution in human health. Pharmaceuticals analytical techniques explain the process or various processes for the identification and quantification of a substance, the determination of the composition of pharmaceutical solution or mixtures or the composition of chemical compounds used in the production of pharmaceutical products. Different chemicals and instrumental methods were developed at regular intervals to enable the drugs to fulfill their purpose, which involved drug presumptions. The constituents observed include processed impurities, chiral drugs, residual solvents, degradation products, extracts as preservatives, extractable from the container, and the production process, drug product pesticides and metabolites from the plant source. Analytical instrumentation and methods play an important role in pharmaceuticals. The review covers a variety of analytical techniques such as titrimetric, particle size analysis, melting and boiling point, disintegration, dissolution, chromatography (HPLC, GC-MS) and spectroscopy (IR, UV-Visible, AAS) methods that have been applied in the analysis of pharmaceuticals according to pharmacopoeias.

Key word: Revolution, Identification, Impurities, chromatographic, spectroscopic.

INTRODUCTION

Guided by pharmacology and clinical sciences, and driven by chemistry, pharmaceutical research in the past has played a crucial role in the progress of development of pharmaceuticals. Contributions to chemistry, pharmacology, microbiology and biochemistry set a standard in the discovery of drugs where new drugs are not only produced by chemists' imagination, but these new drugs are the result of the exchange of ideas between biologists and chemists. The process of drug development begins with the invention of a drug molecule that has shown therapeutic value in fighting, controlling, checking or curing disease. According to Vallagaleti et al (2003), the synthesis and characterization of such molecules, known as active pharmaceutical ingredients (APIs) and their analysis and therapeutic efficacy data for preliminary safety, are a prerequisite for drug candidate detection [1]. Investigations related to pre-drug discovery are based on information on the primary causes of disease treatment, how genes are changed, the causes of the disease, protein and the interaction of the invading cells, and the changes brought about by these infected cells, and how they affect these cells. Based on this information, a compound has been developed that interacts with the infected cells and may eventually discover and develop drug molecules or active pharmaceutical ingredients (A.P.I), to understand the research and development process. Composite that is turned into a drug molecule proves that it is absorbed into the bloodstream, delivered to the body's proper function, sufficiently metabolized and non-demonstrating toxicity, thus, considered safe and successful. can go. After the composite is finalized, the organism is tested for toxicity studies, toxicity and carcinogenicity tests after the in vitro study. Regulatory authorities allow for clinical trials after they have passed pre-clinical tests. Clinical trials check whether the drug is working in the proposed system, its optimal dosage and schedule, while the last two stages produce statistically significant data about the drug's risky association regarding efficacy, safety, and overall benefit. This phase determines the drug's potential interaction with other drugs and monitors the long-term viability of the drug. After successful completion of clinical trials, the drugs were introduced to the market for patients. Various guidelines related to chiral drugs have been published that encouraged the development of a single enantiomer drug for pharmaceutical manufacturers [2-4]. The quality of chiral drugs was determined by the guideline of the International Conference on the Harmonization of Technical Requirements in the Human Use for Pharmaceuticals Registration [5]. Applicants in the guideline are advised to treat other enantiomers as immature, and the identity test will enable them to distinguish both enantiomer and racist mixes. Providing equipment for efficient quality systems is essential to ensuring a safe and accurate production process. However, inadequate-process control may result in products that suffer from surface irregularities [6-7]. Finished products may contain particles of unknown foreign substances. Foreign matter should be identified, and its source should be defined to prevent further contamination. According to Pajander et al (2013), the use of analytical techniques requires the identification of foreign substances from dosage forms and providing efficient detection methods [8]. The drugs that are marketed may have different dosage forms. The formation reports of Pifferi et al (1999), can be classified according to the route of administration [9]. The information on pharmaceutical development provides the scientific rationale for the development and justification of the formulation for a suitable dosage form. Regulatory guidance provides only a limited description of the need for data sets related to drug development [10], but more detailed data are available for toxicological assessment of excipient [11]. Excipient are the major fraction of dosage forms that act as a weakening to allow proper formulation of tablets and casing to protect the tablet from unwanted organoleptic properties of the drug substance. Solid state reactions may occur in the form of a dose when the drug is reactive and may be accelerated by physical and chemical interactions with the external. In some cases, immature individuals do not interact chemically but promote the degradation of drug substances [12]. For example, primary and secondary amines can respond to lactose, glucose, and maltose in the formation of glycosylation [13]. Analytical investigation of bulk drug components, intermediates, pharmaceutical products, formulations of drugs, impurities and degradation products and their metabolic biological samples is very important in pharmaceutical research. This review significances the introduction of different analytical instrumental techniques and their related analytical methods in pharmaceutical industries.

ANALYTICAL INSTRUMENTS

Titration

Titration is the process by which the concentration of an unknown solution is determined against a known solution with the help of indicator. The origins of the titrimetric method of analysis go back somewhere in the mid-18th century. It was 1835 when Gay – Lussac invented the volumetric method that subsequently led to the rise of word titration. With the development of functional group analysis methods, titrimetric methods have proven to be useful in speed measurements that are applied to establish response rates. There are many benefits associated with this approach, including time and labor savings, high accuracy and the need to use reference standards. According to Matei et al (2008), to conducted titrimetric has been used in the past for the evaluation of pharmaceutical products by application in drug degradation [14].

Particle size analysis

Particle size analysis is the collective name of the technical procedures or laboratory techniques which determine the size range and the average or mean size of the particles in a powder sample. Particle size analysis is an embodiment of particle science, and its determination is usually performed in the particle technology. The particle size can have considerable important in several industries including pharmaceutical, the chemical, mining, forestry, agriculture and aggregate.

Melting and boiling point

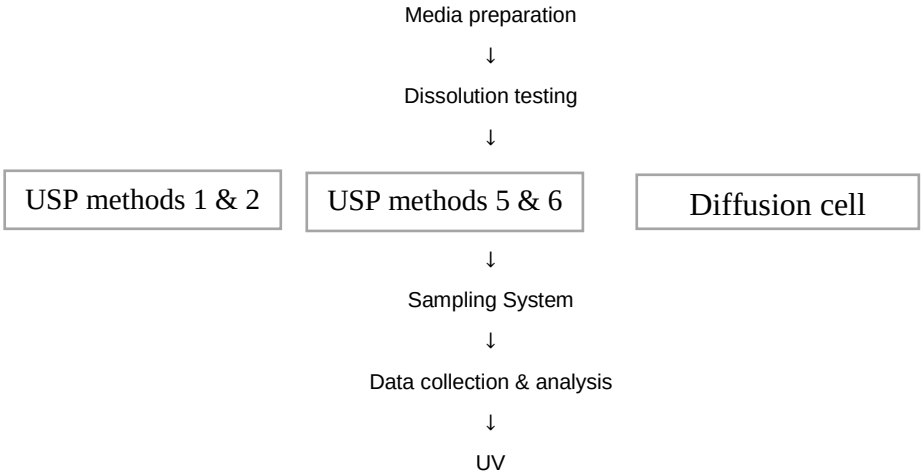
The normal melting point of a solid is defined as the temperature at which the solid and liquid are adjusted to the total pressure of 1 atmosphere. The melting point can be used to identify a substance and to identify its purity. The melting point range of 775^{o}c indicates that the substance is impure. The temperature range/ point of a laboratory distillation of an oil/liquid from start until evaporation is complete. The boiling point of organic compound can give important information about their physical properties and structural characteristic. Boiling point helps identify and characteristic a compound. A liquid boil when its vapor pressure is equal to the atmospheric pressure.

Disintegration

Standard procedure is the process by which a solid oral dosage form is dissolved in water. (15 minutes for uncoated tablets, 30 minutes for film coated tablets and hard gelatin capsules, 60 minutes for other coated tablets). The disintegration test is a measure of the time required under a given set of conditions for a group of tables to disintegration into particles which will pass through a 10 mesh screen. Disintegration is an important quality control test today. In future disintegration testing could become a release test for formulations with API- controlled dissolution. Disintegration testing can save time & cost for quality control department in the pharmaceutical industry due to its simplicity.

Dissolution

Dissolution is the process by which a solid drug substance dissolve in a water bath temperature 37^{o}C.



For the dissolution of solids, the process of dissolution can be explained as the breakdown of the crystal structure into individual ions, atoms or molecules and their transport into solvent. Dissolution process is of fundamental importance to the description of numerous natural processes on earth and it is commonly utilized by humans. Dissolution testing is widely used in the pharmaceutical industry for optimization of formulation & quality control. It also used to predict the in vivo performances of certain product.

Chromatography

Thin Layer Chromatography

Thin layer chromatography is a rectangular piece of glass plate, coated with a thin layer of silica. Applied a spot of the reaction mixture just above the base of plate and placed the plate in a jar that contained an appropriate organic solvent with just enough the volume to sink to the lower end of the plate. Gradually by capillary action, the solvent started rising the silica plate and see the reaction mixture separated into 3 steps with distinct colors by the time the solvent had reached the solvent front mark. TLC is a powerful addition to the screening of unknown substances in bulk drugs [15]. Different drug impurities were identified and determined using TLC [16].

High-performance liquid chromatography (HPLC)

HPLC is a separation technique. Separation of a wide variety of compounds: organic, inorganic, biological compounds, polymers, chiral compounds, thermally labile compounds, small ions to macromolecules. It has two phases. Mobile phase and stationary phase where Mobile phase carry the solvent and stationary phase separate the molecules/compounds. Separation occurred based on flow rate as different flow rates for the different components. HPLC instrumentation includes a pump, injector, column, detector and data acquisition and display system shown in figure 1. It can be detected very small amount solvent & Better resolution of compound from the column. According to USA pharmacopeia (1980), HPLC methods founded for the first time for trail of bulk drug materials [17]. It has become the preferred method of quality control and assurance at many levels of analytical support within the pharmaceutical industry [18]. HPLC has been applied for the drug analysis as well as for pharmaceuticals impurities analysis [19-20].

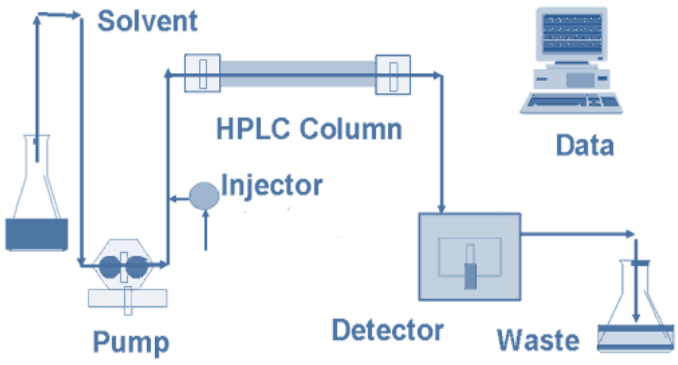


Fig. 1: HPLC (https://images.app.goo.gl/6wSrMRzfsxWEYuVMA)

Gas Chromatography

A gas chromatography (GC) is an analytical instrument that measures the content of various components in a sample. The sample solution injected into the instrument enters a gas stream which transports the sample into a separation tube known as the "column." (Helium or nitrogen is used as the so-called carrier gas) shown in figure 2. Different elements are separated inside columns. The detector measures the amount of material coming out of the column. In order to measure a sample with an unknown concentration, a standard sample with known concentration is injected into the instrument. The standard sample peak retention time (appearance time) and area are compared to the test sample to calculate the concentration. Gas liquid chromatography plays an important role in pharmaceutical product analysis [21]. Gas chromatography is also an important tool for analyzing drug impurities.

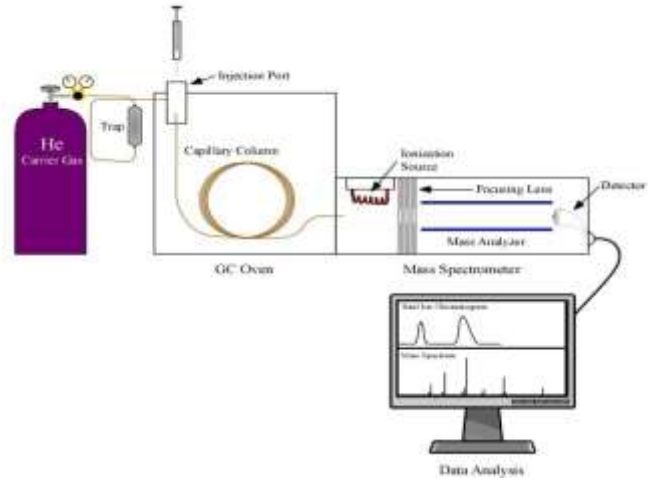


Fig. 2: Gas Chromatography (https://images.app.goo.gl/r4B7go2v1SAG46VA9)

Spectroscopy

Atomic absorption spectroscopy

Atomic absorption spectroscopy is a technique that studies the absorption of electromagnetic radiation related to molecular structure. Atomic absorption spectrometers have 4 principal components light source (usually a hollow cathode lamp), An atom cell (atomizer), monochromator detector, and read out device shown in figure 3. It is a technique to measure the concentration of different elements in the sample by their light absorption. Atomic absorption spectroscopy is based on the principle that when a beam of electromagnetic radiation passes through a substance, radiation can either be absorbed or transmitted, depending on the wavelength of the radiation. Radiation absorption can increase the energy of the molecule. The energy received by the molecule is directly proportional to the wavelength of radiation. The increase in the energy of the molecule leads to the electronic excitations where electrons jump to higher energy levels. A certain wavelength that a given molecule can absorb depends on vibrational, or rotational or electronic state changes.

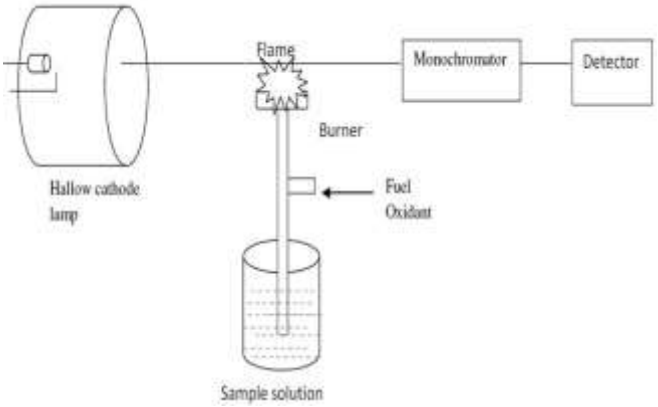


Fig. 3: Atomic absorption spectroscopy (https: //images. app. goo. gl/ 6FLRTq9rp62)

IR spectrophotometer

Infrared spectroscopy is spectroscopy related to the infrared region of the electromagnetic spectrum which is longer with longer wavelengths and lower frequencies than visible light. it covers a wide range of techniques, mostly based on the absorption spectrum. As with all spectral techniques, it can be used to detect to functional group and study chemicals. A common laboratory device that uses this technique is a Fourier transform infrared spectrometer. Diagram of IR spectrophotometer shown in figure 4.

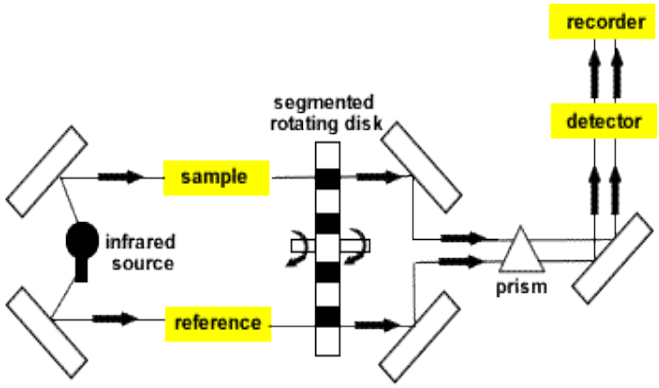


Fig. 4: IR spectrophotometer (https://images.app.goo.gl/pXkbgcouUiWPBkCS8)

UV-Visible spectrophotometer (10nm ≈ 400nm)

UV spectroscopy obeys the Beer-Lambert law, that is to say: when a beam of monochromatic light passes through a solution of an absorber, the rate of radiation intensity decreases with the density of the absorbing solution proportional to the concentration of the solution as the incident radiation. It is clear from the Beer-Lambert law that the number of molecules is higher absorbing light of a given wavelength, the greater the extent of light absorption. This is the basic principle of UV spectroscopy. Its cell is called quartz cell. Instruments for measuring the absorption of U.V. or visible radiation are made up of the following components (shown in figure 5);

1. Sources (UV and visible)

2. Wavelength selector (monochromator)

3. Sample containers

4. Detector

5. Signal processor and readout

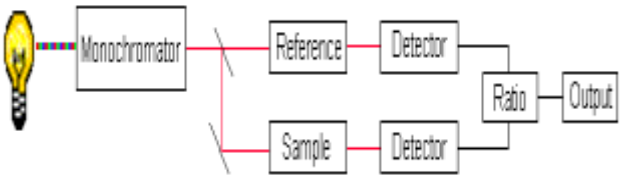


Fig. 5: Schematic Diagram of UV-Visible spectrophotometer

CONCLUSION

The main goal of pharmaceutical medicine is to serve the human being to prevent them from possible illness or disease. For the medicine to fulfill its intended purpose, they must be free from uncleanness or other interference that can harm humans. This review aims to focus on the role of various analytical instruments in the field of pharmaceuticals, and to provide a detailed literature survey of instruments involved in pharmaceutical analysis. The review also highlights the progress of strategies, from the old titrimetric method to advanced hyphenated technology.

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