

Analytical approaches in the pharmaceutical industry



**ASSIGN
BUSTER**

Miracles do happen and chances of happening such events are rare.

Scientific discoveries have also seen such miracles. The approach and efforts required in scientific happenings are based on basic principles. The mode of application of these established principles differ from one stream to another stream of scientific disciplines. The principle of chemistry and physics are amalgamated to give rise to number of measuring devices. These devices are further restructured to suit application.

Analytical chemistry can be defined as the science and art of determining the composition of materials in terms of their elements or compounds contained ¹ in it. Qualitative analysis gives useful details from which functional groups, structural features, atomic species or molecular species. Quantitative analysis gives numerical data in units i. e. percentage, parts per million, moles per liter etc. In above two types of analysis, the required data is obtained by measuring a physical property which is characteristically related to respective component of interest i. e. the analyte ². The most important aspect of analysis is quantitative analysis. The techniques of analytical chemist are of vital importance to the drug and pharmaceutical industries. Products are usually complex organic compounds or mixtures. Drugs prepared for human consumption requires strict standards of product quality be established and maintained.

In past, methods of biological assay were often the only measure of product activity available. With the advent of modern instrumentation, techniques of analyst became more versatile and less time consuming, and quantitative analysis supplemented and sometimes replaced biological assay.

In those instances where it is possible to establish a rigorous correlation between biological activity and chemical composition of product, analysis can be invaluable in controlling manufacturing operations as well as in determination of product purity and activity.

It is noted that the progress and advancement of analytical chemistry depends to a greater extent upon an intelligent application of the fundamentals of physical chemistry and close relationship between physical and analytical chemistry.

Recent rapid progress in physical methods of analysis, in many instances, resulted from pioneering investigations of scientists, principally physicists.

In 1930 Willard recognized the demands being placed on analytical chemistry by rapid industrial progress. A parallel recognition of importance of analytical chemistry to industry occurred in Europe in same year.

Churchill states that contribution of the analytical chemist to research program will be most effective if he is given the opportunity to participate while the program is being planned.

In 1940s several direct reading quantitative spectrophotometers were reported. In these instruments the emitted spectral energy of certain chosen lines is transformed to a proportional electrical output by photomultiplier tubes. By suitable amplification and with appropriate recording devices, percentages of the constituents present are automatically recorded. The outstanding advantage of such equipment is its ability to reduce the time requirement for performing an analysis.

New information made available by combining various tools of analytical chemist, has been described in several articles.

The methods of analysis used to solve industrial problems may be classified as:-

1. Fully developed, generally accepted methods of analysis.
2. Generally accepted methods which are adapted to make them suitable for the problem.
3. New methods which must be developed when available ones are not adequate.

Industrial analysis is defined as the utilization of chemical and physical techniques for solving problems arising in industry.

In some industrial processes it is desirable to obtain a very rapid or continuous analysis of a product or mixture. Considerable progress has been made in developing automatic method of analysis to fulfill this need. While it has not often been possible to automate entire procedures, from sampling to recording of results many examples of partly automated analytical operations can be cited.

Factors pertinent to evaluation of analytical methods in each of these groups were discussed in the present section.

A method of analysis is standard or accepted only in the sense that a number of analysts have judged it to be adequate for obtaining certain analytical information.

Ideally, analyst views the standard method as a “ best approach” rather than an obvious solution. If satisfactory results are obtained the method can be applied to the sample under consideration with some assurance that the experimental procedure is not at fault. The analyst himself should perform this part of work even if future measurements will be carried out by technicians or laboratory assistant. Only by performing the manipulation and observing the reaction can the analyst forming thoroughly acquainted with the details of an analytical procedure.

The advisable method is when it appears to give satisfactory results, include consideration of interfering elements or compounds and determination of blank. While interferences which prevent a method from working properly are readily detected, those which produce a constant error in the analytical result are much more insidious and seldom apparent. Determination of a blank eliminates possible source of constant errors, such as contaminants in reagents and uncorrected background in instrumental measurements.

In many standard methods the design and dimensions of the equipment are critical, particularly when properties of material rather than its composition is being studied.

Many modification of an analytical method are possible and each problem or sample dictates the changes required to make the method effective.

In some methods modification involves change in equipment or technique. For example, numerous spectrographic procedures have been developed for analyzing the metallic contaminants or additives in lubricating oils.

Methods, which fail or suffer loss in sensitivity when certain interferences are present, may sometimes, need to be modified by introducing an additional step in the procedure which eliminates or deactivates the interfering element.

Once a procedure has been adapted to a particular problem it may be evaluated in the same manner as a standard method. The usual precautions related to proper manipulation and standardizations, avoiding contamination and blank determinations must be observed.

When problem is confronted which cannot be solved with established methods of analysis, it becomes necessary for analyst to create and develop new analytical procedures. This situation arises when any or all of the following factors are in effect.

1. The substance sought has not previously been determined, when no methods are now available for all elements.
2. The substance sought is a component of a mixture not previously analyzed. Any other element or compound present in a mixture may invalidate established methods of analysis by interference effects. Sometimes the component producing the interferences can be eliminated and a modified form of the original procedure can be used, as already described.
3. Higher order of sensitivity is required when component sought is present in small quantity (mg). A method capable of analyzing in desired concentration range must be developed.

4. Problems arising in industry are complicated by sample limitations. Often the sample is available in very small amounts and special techniques are required for gaining maximum information from a minimum quantity of material.
5. Analysis must be non-destructive. At times it is required that the sample remain unaltered by the analytical procedure. For example compositional information on an expensive finished product is required, a non-destructive analytical method.
6. Speed or time is critical requirement when conventional methods cannot complete an analysis within a prescribed time requirement, faster methods must be developed.

Analytical Chemistry importance in different scientific areas:

Importance of analytical chemistry in related scientific areas can be demonstrated by considering analytical chemistry's impact on clinical analysis, and in pharmaceutical research and in quality control.

- Sensitive chemical and instrumental tests were advised in order to detect abnormal and normal components of body fluids.
- Blood and urine samples are determined for percentage of glucose, urea, nitrogen, protein, sodium, potassium, calcium, uric acid etc.
- Similarly, the quality of manufactured drug in tablets, solution and emulsion form must be carefully controlled in pharmaceutical industry, otherwise the drug can itself affect the therapeutic value. In other pharmaceutical studies, it is important to establish properties and

therapeutic value of a drug before the drug is approved and made available to the public.

Analytical Techniques:

Few of medicinal products were still being analyzed by time-tested procedures of gravimetric and also titrimetric procedures. A wide diversity in different type of analytical techniques has been characteristic of assay methods for pharmaceutical products. Different analytical techniques were been employed for estimation of wide variety of components in the formulation:-

1. Titrimetric and gravimetric method
2. Colorimetric and UV spectrophotometric method
3. Paper chromatography
4. Preparative thin layer chromatography
5. Column chromatography
6. Ion-exchange chromatography
7. Flame photometry and atomic absorption spectrometry.

Variables in Quantitative Analysis:

- Inhomogeneity of the medicament
- Sampling error
- Preparation of samples such as extraction
- Precision, accuracy and ruggedness of the method
- Random error including that of the operator.

Newer Analytical Techniques:

As technology is developing, a number of new drugs are launched in the market and it is essential to develop new methods of analysis.

It is necessary to do if;

1. No analytical methods are available for a drug in official books such as pharmacopoeias.
2. No literature reveals methods for estimation of drugs.
3. Analytical method available only for single drug in a combined form of drug.
4. No method reported for the estimation in biological fluids.

NEED OF ANALYTICAL APPROACHES IN PHARMACEUTICAL INDUSTRY

The pharmaceutical industry has always had in place a series of process controls which assures the integrity of the end product. “ A simple way of looking at it is that the Food & Drugs Act & Regulations are merely an auditing mechanism to quantify that industry has sufficient process controls and documented procedures in place to ensure they are in complete control of every aspect related to drug manufacturing,”

There are in essence, three pillars to drug manufacturing and distribution:

1. Quality Assurance (QA)
2. Good Manufacturing Practices (GMP)
3. Quality Control (QC)

Quality Assurance is ensuring that you get what you pay for. It is the insurance policy for the manufacturer." As a brief overview, the GMPs are part of Quality Assurance and ensure that drugs are produced consistently and are controlled at each and every step. QC is a part of Good Manufacturing Practices and is responsible for sampling and also for testing. It examines and ensures that all aspects of product from raw materials and integrity of the product itself to the packaging materials and insert, meet their specifications. It encompasses testing of the end product and all of its primary ingredients. QA covers documentation of all of the procedures that have taken place from start to finish of entire process. This, in combination with QC's sampling and testing, allows QA to ensure product's integrity, purity and potency have not been compromised and it has satisfied all requirements. When QA is completed and satisfactory, the final step is permitted allowing a product to be released for sale to the consumer.

But, their job doesn't stop here. Since Quality Assurance is responsible for assuring that final product is meeting quality, consistency and integrity for its intended use, it must also account for when the product leaves the manufacturing site. Thus, QA is also responsible for ensuring that appropriate arrangements have been made with distributors and warehouses to guarantee that the product is handled, stored and shipped in such a way that its quality is maintained for the duration of its approved shelf life.

The overall time required for development of a pharmaceutical from Discovery Research through to the Regulatory Review Phase. There is clear evidence that this can in some cases take upwards of 15 years with costs reaching into millions of dollars. With this level of Research and

<https://assignbuster.com/analytical-approaches-in-the-pharmaceutical-industry/>

Development investment, the industry has no intention of allowing a breakdown in final stages of manufacturing and distribution process. Therefore, before a product actually reaches market, QA involvement is also the key in the registration dossier preparation. A portion of this dossier contains a Master Production Document (MPD) which outlines exactly how the product will be manufactured. Within this MPD, a manufacturer defines clear specifications for all raw materials, packaging materials, in-process and finished product along with the sampling procedures and also Standard Operating Procedures (SOPs) related to critical processing. The issuing of a Notice of Compliance and a Drug Identification Number are contingent on a complete and acceptable Master Production Document.

Then manufacturing license holders are also responsible for conducting an annual self-inspection and documenting their procedures and processes are in compliance with the requirements of the GMPs.

If the manufactured product is stored in bottles (syrups), fabricating, packaging/labeling, importation, distribution, wholesale (Schedule C, D, F or G products) or testing of pharmaceutical products must first hold an Establishment License issued by Government.

PRESENT STUDY:

Development of new drugs, drug manufacturing is dependent on drug analysis. Pharmaceutical companies depend upon drug analysis quantitatively to conform that the raw materials used, in-process compounds and final products manufactured were meeting the required specifications.

New drug formulations and new drugs were introduced into the market at <https://assignbuster.com/analytical-approaches-in-the-pharmaceutical-industry/>

increased pace compared to earlier days, as the technology is developed. These formulations and drugs were either new chemical entities or partial structural modifications of existing drugs or new dosage forms. Frequently, it happens that the new drugs inclusion in pharmacopoeias will be delayed because of several reasons. Hence these standards or the analytical methods for these drugs may not be available in pharmacopoeias. Hence it is essential to develop new methods of analysis for these drugs. Based on this, few combinations were selected for the present studies which were currently marketed from Anti Hypertensives ¹⁷⁻²² , Anti HIV ²³⁻³⁵ and Non Steroidal Anti Inflammatory Drugs ³⁶⁻⁴⁷ .

1. Amlodipine Besylate
2. Telmisartan
3. Lamivudine
4. Zidovudine
5. Thiocolchicoside
6. Etoricoxib

Literature survey was performed extensively and it was found that spectrophotometric methods were reported and also HPLC methods were reported for the determination of these drugs from their biological fluids. However, there were no reports found for their quantitation by HPLC methods from their formulations. Hence it is essential to develop newer rapid analytical methods ³⁻¹⁶ on HPLC.