



ADVANCES IN PHARMACEUTICAL RESEARCH SCIENCES- AN REVIEW

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Abstract: This overview describes the various advances in pharmaceutical advances in researches. This minireview summarized numerous examples to demonstrate the application of electrochemical techniques for pharmaceutical and drug analysis. Special attentions have been committed to the voltametric and potentiometric strategies. A section devoted to the use of the electrochemical detectors in addition to flow system was also presented. Finally, we briefly outline future pattern of the electrochemical methods for drug evaluation. Electroanalysis is employed as an another or complementary technique to spectrophotometric and separation techniques due to its high perceptivity, speed of analysis, reduction in solvent and sample consumption, and low operating cost compared to other analytical techniques. Capillary electrophoresis (CE) has a momentous character in drug discovery and manufacturing process and has ability to develop further, because of new traits which can give vastly delicate and high throughput analysis. This review illustrates current packages of CE in pharmaceutical analysis. The history, principles, instruments, and traditional modes of CE are briefly described. The position of the analytical strategies and their validations has been essential in quantification of medication from their dosage bureaucracy or organic samples in current years. Development of analytical strategies coupled with every different, is beneficial for the research of conduct of medication or metabolites or impurities, and is likewise a beneficial device for touchy detections. The current roles of spectroscopy, chromatography, titrimetry, electrochemistry and capillary electrophoresis had been defined here. The improvement of the prescribed drugs added a revolution in human health. These prescribed drugs might serve their meant most effective if they're unfastened from the impurities and are administered in suitable amount. To make tablets serve their motive diverse chemical and instrumentation approach have been advanced at normal durations which can be worried withinside the estimation of medication. These prescribed drugs might also additionally broaden impurities at diverse ranges in their improvement, transportation and garage which makes the pharmaceutical volatile to be administered consequently it should be detected and quantitated. For this analytical instrumentation and strategies performs an essential position. The overview highlights type of analytical strategies along with titrimetric, chromatographic, spectroscopic, electrophoretic, and electrochemical and their corresponding strategies that has been carried out withinside the evaluation of prescribed drugs.

Keywords: Electrochemical Techniques, Titrimetry, Spectroscopy, Electrochemistry, Capillary Electrophoresis (CE), Chromatography.

1. INTRODUCTION

The pharmaceutical sciences represent an evolving and highly dynamic field, and two overreaching trends show an increased effort to develop biologic-based drugs and creating more specific or targeted drug delivery techniques. Some recent developments are the development of spatial aggregation propensity for detecting protein aggregation, advances in drug-delivery technologies involving microencapsulation and nanocoatings, and tools to understand the risk of nanomaterials in drug-delivery systems. Electrophoresis is a separation technique that is based on the differential migration of charged compounds in a semi-conductive medium under the influence of an electric field. Capillary electrophoresis (CE) is a powerful separation technique that is widely used in research and development (R&D), quality control (QC), and stability studies of pharmaceuticals. CE offers several advantages over high-performance liquid chromatography (HPLC), a technique commonly used in pharmaceutical analysis. These include simplicity, rapid analysis, automation, ruggedness, different mechanisms for selectivity, and low cost. Furthermore, it offers higher efficiency and thus greater resolution power over HPLC even if only a small sample size is available. These advantages are likely to lead to even greater use of CE in R&D, QC, and stability studies of pharmaceuticals. CE has been found particularly useful for separations of peptides, proteins, carbohydrates, inorganic ions, chiral compounds, and in numerous other pharmaceutical

applications. As directly associated with patient health and wellbeing, the assurance of pharmaceutical products quality is considered crucial. Therefore, the quality control is considered the corner stone for many processes starting with but not restricted to raw materials analyses, purification, drug manufacturing, patch assays, and many others including research and development disciplines. For instance, the field of pharmaceutical research is progressively developing and the design, synthesis, and development of new or existing drugs push an extra pressure of enhancing the present methods or developing new ones. This is true for the uniqueness of the drug molecules or dosage forms for the capability of being very simple inorganic salts (e.g., potassium chloride) to a very complexed monoclonal antibodies or even more complicity with the pharmacogenomic therapeutics. Consequently, this required a very sensitive and selective analytical techniques to be utilized. Hence, in this review, the authors highlight the analytical techniques those are commonly utilized in pharmaceutical drug analyses.^[1]

Analytical techniques for pharmaceutical analysis

The analytical techniques used in pharmaceutical analysis are listed below:

A. First technique: Titrimetric ^[1,4,5,6]

Titrimetric methods are utilized in pharmaceuticals analysis due to their less time consumption, high precision and no want to reference standards. Indeed, it is a completely vintage method if compared with the other analytical techniques, the titrimetric system received unique interest in at the same time as implemented in the rheology and kinetics because of the usage of the functional groups involved in the drug molecules. Origin of the titrimetric technique of evaluation is going returned to someplace withinside the center of the 18th century. It became the yr 1835 while Gay- Lussac invented the volumetric technique which sooner or later cause the starting place of time period titration. It is obvious from desk 6 that during many instances titrimetric strategies remains technique of desire for plenty chemists. Although the assay technique could be very vintage but there are symptoms and symptoms of a few modernizations, i.e., spreading of non-aqueous titration technique, increasing the sector of utility of titrimetric strategies to (very) vulnerable acids and bases in addition to potentiometric give up factor detection enhancing the precision of the strategies. With the improvement of purposeful institution evaluation approaches titrimetric strategies were proven to be useful in kinetic measurements that is in tern implemented in organizing response rates. There are many benefits related to those strategies which encompass saving time and labor, excessive precision and the reality that there may be no want of the use of reference standards. In beyond titrimetric strategies were used for the dedication of captopril (Rahman et al., 2005a), albendazole (Basavaiah and Prameela, 2003) and gabapentin (Sameer et al., 2011) in business dosage forms. Sparfloxacin (Marona and Schapoval, 2001) become dedication via way of means of non-aqueous titration technique. In addition to its utility in drug estimation titrimetry were utilized in beyond for the estimation of decay merchandise of the pharmaceuticals (Matei et al., 2008).

B. Second technique: Electroanalytical ^[10,11]

Electrochemical analytical method is one of the inexpensive, simple, and touchy gear that possesses low restriction of detection as an additional benefit. The voltammetric techniques used these days in analytical chemistry laboratories have been made feasible via way of means of latest advances in instrumentation, automated processing of analytical data, and in particular, revolutionary electrochemists. The time period running electrode is reserved for the electrode at which the response of hobby occurs. Solid or mercury-primarily based totally electrodes are used as running electrodes in voltammetric strategies. In general, stable electrode substances have the benefit of being greater routinely stable, and that they offer a bigger anodic variety than mercury-primarily based totally electrodes. Also, the dealing with of stable electrodes is tons less complicated such that they'll quite simply be implemented in waft streams because of their mechanical balance and hardness. The area of changed stable electrodes has end up very famous with a huge variety of programs in industry, best manage of medicine and food, dedication in pharmaceutical dosage forms, environmental monitoring, and so forth. The capability variety over which voltammetric strategies may be used relies upon at the stable electrode cloth, the solvent, the helping electrolyte, and pH of the studied solution. Solid electrode voltammetry is used in large part for the oxidation of materials at pretty nice potentials in addition to for extremely without problems reproducible materials. The overall performance of the voltammetric technique is strongly encouraged via way of means of the cloth of the running electrode.

C. Third technique: Chromatographic ^[9]

The chromatographic techniques applied in drug analyses may be enclosed via three major essential techniques. These are:

a. Thin-layer chromatography: Despite the Thin Layer Chromatography (TLC) is taken into consideration as antique tool, it still be utilized in habitual laboratory tactics particularly when utilized in analytical drug assays.

b. High performance liquid chromatography: No writer can write approximately analytical strategies for pharmaceutical merchandise and pass the High- Performance Liquid Chromatography (HPLC). This approach became first off added to assay bulk drug parts in the United States Pharmacopoeia (USP) withinside the year of 1980.

c. Gas chromatography: Even the Gas Chromatography (GC) is limited for unstable drug molecules, undoubtedly, this approach is taken into consideration very touchy with effective separation capabilities. This results in the large usage of this sturdy analytical approach to come across very hint quantities of even picograms of drug substances after setting apart them.

D. Fourth technique: Capillary Electrophoresis ^[3,4]

Capillary electrophoresis (CE) was developed from combining several features of different methods including the principle of gel electrophoresis, the fused silica capillary of gas chromatography (GC), and the highly sensitive detectors of high-performance liquid chromatography (HPLC). Separation in CE is based on different mobility of analytes under an electric field, which occurs in a capillary filled with buffer. Unlike other media (e.g., paper, agarose, and polyacrylamide gel), electrophoresis in a capillary can use a high voltage (up to 800 V/cm) due to the physical properties of fused silica capillaries. A large surface area to volume ratio of a capillary provides effective heat dissipation. The small dimension of a capillary requires small amounts of samples and buffer and the automation of CE requires less time and labor. Additionally, the high separation efficiency [number of theoretical plate (N) > 10,000], the on-column detection, and the various modes of CE make the technique attractive for solving challenge problems.

The principle of CE is based on the different migration of solutes in an electric field, and electrophoresis is performed in narrow-bore capillaries filled with electrolyte. The mobility of analytes depends upon their sizes, charges, and degree of ionization, viscosity, temperature, and dielectric constant of the background electrolyte (BGE). Upon application of voltage, analytes are driven by two forces, the electrophoretic migration and the electro-osmotic flow (EOF). Capillaries are commonly made from silica; therefore, the inner surface can yield the multiple ionization of silanol groups ($\text{pH} = 1.5$) at any $\text{pH} > 3.0$ (13,14). These silanol groups ionize in aqueous electrolyte, causing negative charges during a separation at the inner wall surface and the EOF. Controlling the EOF can significantly influence the efficiency and selectivity of a separation, because EOF is a main driving force in CE that enables the migration of analytes along the capillary. Factors affecting EOF include electric field, pH, and concentration/ionic strength of the BGE, additives, temperature, and capillary coatings. Unlike pressure-driven forces (i.e., laminar flow), EOF provides a flat flow profile, which gives narrow peaks with a high number of theoretical plates. Additionally, EOF enables the simultaneous separation of cations, anions, and neutral compounds. Analytes are usually introduced at the anode and are detected at the cathode, and cations migrate first with the highest velocities toward the cathode by the electrophoretic force and the EOF. Neutral compounds migrate with the same velocity of the EOF and are detected as one peak. Lastly, anions migrate by the force difference of the EOF toward the cathode and the electrophoretic flow from the anode in the opposite direction.

E. Fifth technique: Spectroscopy ^[8]

Another essential organization of techniques which unearths an essential region in pharmacopoeias are spectrophotometric techniques primarily based totally on herbal UV absorption and chemical reactions (Gorog, 1995). Spectrophotometry is the quantitative dimension of the mirrored image or transmission houses of a fabric as a feature of wavelength. The blessings of those techniques are low time and labour consumption. The precision of those techniques is likewise excellent. The use of UV-VIS Spectrophotometry particularly implemented withinside the evaluation of pharmaceutical dosage shape has improved swiftly over the past few (Tella et al., 2010; Venugopal and Sahi, 2005; Sharma et al., 2008; Ieggli et al., 2005). The colorimetric techniques are typically primarily based totally on the subsequent aspects:

- Complex-formation reaction
- Oxidation-discount process
- A catalytic effect

a. UV- Spectroscopy:

Ultra Violet Visible (UV-Vis) spectroscopy is a worldwide spread technique employed in a very simple, reliable, fast, and relatively inexpensive utilized in both quantitation and qualification of pharmaceutical ingredients that possess chromophoric group(s) to be used in the daily laboratory basis works. It is essential to say that colorimetric techniques are frequently used for the assay of bulk materials. For example, the blue tetrazolium assay is used for the willpower of corticosteroid drug formulations (Gorog and Szasz, 1978; Gorog, 1983). The colorimetric approach is likewise exploited for the willpower of cardiac glycosides and is provided in European Pharmacopoeia. Several strategies the usage of spectrophotometry for willpower of energetic pharmaceutical substances in bulk drug and formulations had been stated and info of those techniques are recorded in underneath table.

Reagent Used	Name of Drug	-max	Reference
m-Cresol	Acetaminophen	640	Qureshi et al. (1992)
p-chloranilic acid	Quetiapine Fumarate	520	Vinay and Revenasiddappa (2012)
	Milrinone	519	Siddiqui et al. (2009)
2,3-Dichloro 5,6-dicyano1,4-benzoquinone	Duloxetine	477	Toker and Önal (2012)
	Amlodipine besylate	580	Rahman and Hoda (2003)
Iodine	Flunarizine dihydrochloride	380	El Walily et al. (1995)
	Aripiprazole	400	Helmy (2012)

b. Raman Spectroscopy: [2,3]

Raman spectroscopy end up a famous and capability analytical approach for the evaluation of prescription drugs because of its development. The innovation of laser technology, Fourier Transform-Raman spectrometers with price coupled device (CCD) detectors, ease of pattern education and handling, mitigation of sub-sampling troubles the usage of exclusive geometric laser irradiance styles and invention of various optical additives of Raman spectrometers are individuals of the development of Raman spectroscopy. Transmission Raman Spectroscopy is a beneficial device in pharmaceutical evaluation to cope with the troubles associated with sub-sampling in traditional Raman again scattering. More importantly, the improvement of surface-more suitable Raman scattering (SERS) has been a outstanding development for Raman spectroscopy to be carried out for prescription drugs evaluation because it avoids the inherent insensitivity and fluorescence troubles. As the energetic pharmaceutical ingredients (APIs) incorporate fragrant or conjugated domain names with sturdy Raman scattering activity, Raman spectroscopy is an appealing opportunity traditional analytical approach for prescription drugs. Coupling of Raman spectroscopy with separation strategies is likewise some other development carried out to lessen or keep away from feasible spectral interferences. Therefore, on this review, transmission Raman spectroscopy, SERS, and SERS coupled with diverse separation strategies for pharmaceutical evaluation are presented.

c. Near Infrared Spectroscopy (NIRS): [2]

Near infrared spectroscopy (NIRS) is a fast and non-adverse technique that offers multi element evaluation of virtually any matrix. In current years, NIR spectroscopy has received huge appreciation withinside the pharmaceutical enterprise for uncooked fabric testing, product exceptional manage and procedure monitoring. The developing pharmaceutical hobby in NIR spectroscopy might be an instantaneous result of its principal benefits over different analytical strategies, namely, an clean pattern guidance with none pretreatments, the opportunity of setting apart the pattern size role through use of fiber optic probes, and the expectancy of chemical and bodily pattern parameters from one unmarried spectrum. The principal pharmacopoeias have normally followed NIR strategies. The European (bankruptcy 2.2.40, European pharmacopoeia, 2001) and United States (bankruptcy 1119 United States Pharmacopoeia USP 26 NF 21) deal with the suitability of NIR instrumentation for utility in pharmaceutical testing. NIR spectroscopy in aggregate with multivariate information evaluation opens many thrilling perceptions in pharmaceutical evaluation,

each qualitatively and quantitatively. A variety of guides describing quantitative NIR measurements of lively component in intact capsules were reported (Moffat et al., 2000; Alvarenga et al., 2008; Thosar et al., 2001; Ramirez et al., 2001; Blanco et al., 1999; Blanco et al., 2000; Li et al., 2003; Blanco et al., 1996; Molt et al., 1996; Buchanan et al., 1996; Merckle and Kovar, 1998; Eustaquino et al., 1998; Trafford et al., 1999; Corti et al., 1999; Chen et al., 2001). In Addition to the studies articles many evaluate article has been posted mentioning the utility of the NIRS in pharmaceutical evaluation (Luypaert et al., 2007; Blanco et al., 1998).

d. Nuclear Magnetic Resonance Spectroscopy (NMR) ^[2]

Since the primary file seemed in 1996 (Shuker et al., 1996) describing the usage of NMR spectroscopy to display screen for the drug molecules, the sphere of NMR primarily based totally screening has proceeded promptly. Over the previous couple of years, numerous cutting-edge tactics were supplied and discovered good sized utility in each pharmaceutical and educational studies. Recently NMR unearths its utility in quantitative evaluation for you to decide the impurity of the drug (Mistry et al., 1999), characterization of the composition of the drug merchandise and in quantitation of medication in pharmaceutical formulations and organic fluids (Salem et al, 2006; Reinscheid, (2006), Many evaluate at the utility of NMR in prescribed drugs were posted (Holzgrabe et al., 2005; Malet-Martino and Holzgrabe, U, 2011).

e. Fluorimetry and Phosphorimetry ^[2]

The pharmaceutical industries constantly search for the touchy analytical strategies the usage of the micro samples. Florescence spectrometry is one of the strategies that serve the reason of excessive sensitivity with out the lack of specificity or precision. A sluggish boom withinside the variety of articles at the utility of Fluorimetry (Rahman et al, 2012; Rahman et al., 2009) and phosphorimetry (De Souza et al., 2013; Chuan et al., 2000) in quantitative evaluation of numerous pills in dosage bureaucracy and organic fluids were observed in current past.

f. Liquid chromatography-tandem mass spectrometry (LC-MS/MS) ^[3]

Liquid chromatography-tandem mass spectrometry (LC-MS/MS) gives accurate sensitivity and selectivity for prescribed drugs with none chromophores and fluorophores. LC-MS/MS spectrometry may be used for the detection of hint quantity of compounds and it is able to be beneficial for the identity of pharmacokinetic profile of prescribed drugs. In those days, there are numerous most cancers patients. Rapid and touchy pharmacokinetic evaluation of anticancer capsules are very important for patients. Currently, this technique could be very beneficial in preclinical and scientific studies. The achievement of LC-MS/MS relies upon on pattern preparation, peaks symmetry and ionization parameters. Multiple evaluation can also additionally be carried out with LC-MS/MS. With development in UPLC systems, evaluation time is decreased. LC-MS/MS technique is a completely effective device for lots clinical researches and scientific evaluation.

F. Sixth technique: Localized drug delivery ^[6]

Bingyun Lim, assistant professor in the West Virginia University (WVU) Department of Orthopedics and director of the WVU Biomaterials, Bioengineering & Nanotechnology Laboratory, and his team developed two drug-delivery technologies—microcapsules and a nanocoating- for delivering the drug interleukin-12. The first technology involves the use of microcapsules that can be injected or potentially delivered in a fine-mist spray directly to the site of an injury. The second technology is a nanocoating of interleukin-12 applied directly to stents, pacemakers, pain pumps, artificial limbs or another biomedical device. This approach prolongs the half-life of the interleukin-12. In both methods, because the interleukin-12 is delivered locally rather than systematically, potential side effects are minimized. Li drew his team from the WVU Department of Orthopedics, the WVU School of Pharmacy, the National Institute for Occupational Health and Safety, and the WVU Department of Microbiology, Immunology and Cell Biology. The team has spent the past four years in developing the technology.

G. Seventh technique: Nanotechnology in pharmaceuticals ^[7]

Nanotechnology gives first-rate promise withinside the pharmaceutical industry, however the related chance of nanomaterials continues to be unknown. Researchers on the University of California at Los Angeles (UCLA) and the California Nano Systems Institute (CNSI) lately posted studies that tested the nanoparticle-organic interface to discover the ability dangers of engineered nanomaterials and to discover layout strategies as a way to cause more secure and extra powerful nanoparticles to be used in numerous remedies and products, consistent with an UCLA press release. Nanoparticles can have interaction with proteins, membranes, cells, DNA, and organelles and create nanoparticle/organic interfaces that rely upon colloidal forces and bio-physico-chemical interactions, which in flip can cause the formation of protein coronas, particle wrapping, intracellular uptake, and biocatalytic tactics with favorable or terrible effects. Examining those interfaces permits predictive relationships among shape and pastime to be evolved primarily based totally on nanomaterial residences together with size, shape, floor chemistry, roughness, and floor coatings (3). "What we've mounted here's a blueprint as a way to serve to train the primary era of nanobiologists," stated Andre Nel, crew chief and leader of the department of nanomedicine on the UCLA David Geffen School of Medicine and the California Nano-systems Institute, in a UCLA press release. The paintings is critical for reaching a higher knowledge of the interrelationship among intracellular pastime and characteristic of engineered nanomaterials, which is wanted for nanoparticle drug-transport systems. According to the UCLA release, a great deal of the modern-day information derives from the examiner of tagged or categorized nanoparticles and their results on cells after mobile uptake, with none specific knowledge of whether or not the effects of those interactions can be favorable or not.

H. Eighth technique: Resolving protein aggregation ^[5]

Researchers at the Massachusetts Institute of Technology (MIT) have advanced a laptop model to cope with the problem of short shelf-life for protein-based completely drugs due to aggregation. Most of the aggregation seen in antibodies is due to interactions amongst exposed hydrophobic regions of the proteins. "Drugs are usually advanced with the requirements of the manner effective they will be, and the manner well they will bind to something intention they will be pre-alleged to bind," said Bernhardt Trout, professor of chemical engineering at MIT, in a June 2009 university press release. "The problem is there are all of these issues down the street that were in no way taken into account." The model moreover selects regions responsible for aggregation in area of selecting definitely single sites. Once the hydrophobic regions are identified, researchers can mutate the amino acids withinside the ones regions to decrease hydrophobicity and make the molecule more stable, in step with the MIT release. Using the model, the institution produced mutated antibodies with extensively higher stability (as lots as 50% more than the particular antibodies), and the mutations had no damaging have an impact on their function. The technology may be carried out to screening anti bodies withinside the invention phase.

CONCLUSION:

In this paper, latest research approximately pharmaceutical evaluation were investigated. Chromatographic strategies have acquired awesome hobby for pharmaceutical evaluation with sensitive, selective and transportable properties. It may be coupled with spectroscopic strategies, in order that bodily and chemical properties, kinetic profiles and a hit validation parameters may be obtained. Electrochemistry also can be maximum beneficial technique in analytical chemistry because of improvements in substrate fabrication and technique optimization steps. It permits low chemical utilization and miniaturization gadgets. Hence, it may be implemented in scientific research in destiny with its low cost, dependable responses and user-pleasant gadgets. Today, we're a long way from attaining a systems-degree know-how of human sicknesses and desire that higher small gadgets can be used for the detection of human sicknesses from their organic samples. It will enhance the fulfillment price of remedies of sufferers and forestalls undesirable effects in scientific field.

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