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REVIEW ON DIFFERENT TYPES OF DETECTORS USED IN CHROMATOGRAPHY TECHNIQUES

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Abstract

High Performance Thin layer Chromatography (HPTLC) technique is a sophisticated and automated form of the thin-layer chromatography (TLC) with better and advanced separation efficiency and detection limits. The analytical method should be sensitive, specific, fast and accurate to establish the assurance that the equipments used in manufacturing are free of the unwanted impurity, presence of which may alter the safety and efficacy of the drug product. The developed method was based on RP-HPLC leave-taking and quantification of the drug on C-18 column using a mobile phase at flow rate of 1 ml/ min. Quantitation was attained with PDA detector at 200-400 nm based on peak area with linear calibration curves at concentration ranges 5-25 µg/ml for the drug. The method as per ICH guidelines was validated for specificity, linearity, detection limit, quantitation limit, precision, accuracy, robustness, solution stability, and can be effectively used for routine analysis.

Keywords: RP-HPLC, ICH Guidelines, Antiviral drugs, Precision, Accuracy.

Introduction

Chromatography means – Colour Writing. It is new physical technique of separation, identification, and purification of components of a mixture. It is used in many areas of study particularly in chemistry, biology and medicine. Pigments, dyes, amino acids, vitamins, polymers, etc can be separated by using the chromatography technique. It is often used to detect one or a number of components in a complex mixture. A chromatography detector is a device used in high performance liquid chromatography (HPLC) to detect components of mixture being eluted off the chromatography column. It is used for the purification and separation of organic as well as inorganic substances. Laboratory technique for the Separation of mixtures

Chroma -"color and graphein -"to write". Colour bands - separation of individual compounds. Measured or analysed. The contributions of chromatography to various scientific disciplines and the benefits that chromatography provide to mankind are unparalleled. For example the progress made in the biological sciences such as biotechnology, clinical pharmacology, therapeutics, and toxicology. Chromatography is a separation technique that uses the size, shape, chemical properties or charge of molecules in a sample to separate the sample into its constituent components. All chromatographic systems have a mobile phase that transports the analytes through the column and a stationary phase coated onto the column or on the resin beads in the column.1The power of chromatography comes from its ability to separate a mixture of compounds, or "analytes", and determine their respective identity (chemical structure) and concentration.

Substances are separated based on their differential distribution between two phases. Substances will move with the mobile phase at different rate depending upon their Partition or Distribution coefficients. Physical method of separation that distributes components to separate between two phases moves in a definite direction. Technique in which the components of a mixture are separated based on differences in the rates at

which they are carried through a fixed or stationary phase by a gaseous or liquid mobile phase.

HISTORY

In 1941 Martin and Synge, described the discovery of liquid-liquid partition chromatography and also laid the foundation of Gas liquid chromatography and High performance liquid chromatography.

The first true chromatography is usually attributed to the *Russian-Italian botanist Mikhail Tsvet in 1906*. He used a liquid-adsorption column containing calcium carbonate to separate yellow, orange, and green plant pigments are known as xanthophylls, carotenes, and chlorophylls, respectively [2].

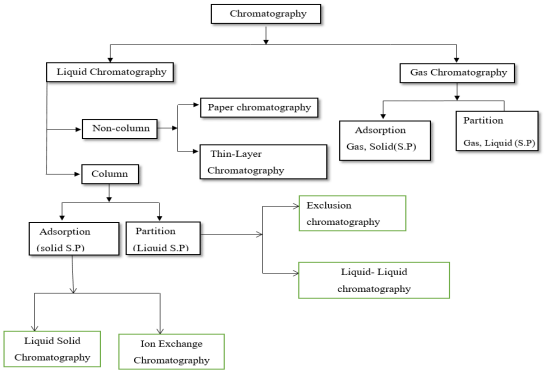
Since about 1969, there has been a very marked revival of interest in the technique of liquid column chromatography because of the development of HPLC by *Kirkland and Huber*. They also introduced the concept of the Height Equivalent to the Theoretical Plate, which has since been adopted as the measure of Chromatographic efficiency. The derivation below follows the same trends that can be found in early texts such as Karger et al. (1973) and Willard et al. (1981), as well as the most recent text by Skoog et al. (2007).

He developed the theory of capiliary analysis by using paper strips while examining wine, milk, alkaloids, dyes and oils among other. His work was an improvement of the work Christian friedrichschonbein, who was his mentor (1799-1868).

He developed technique and coined the term chromatography in the first decade of the 20 century. The earilest hints of applied chromatography principle emerged in the 1800s. German chemist friedlieb and Ferdinand Rung his hade a keen interest the behaviour of coloured eyes and he began to note patterns when they where blotted on filter paper, which he is used to monitor chemical reactions.

The liquid and soild was first discovered by TSWETT in 1903,is probably the OLDEST MODE OF CHROMATOGRAPHY is used to separate analytes of a relatively narrow polarity range from the interfering compounds of different polarity.

Classification of HPLC

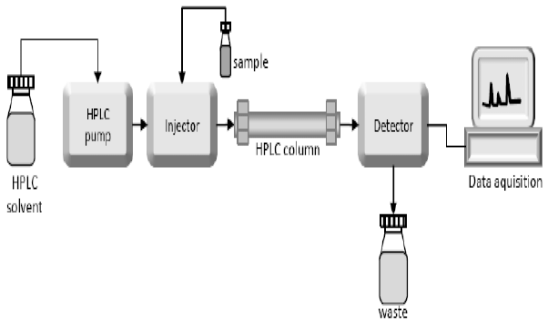


Principle of HPLC

The principle of separation in normal phase mode and reverse phase mode is adsorption. When a mixture of components is introduced into a HPLC column, they travel according to their relative affinities towards the stationary phase.3The component which has more affinity towards the adsorbent, travels slower. The component which has less affinity towards the stationary phase travels faster. The two components have the same affinity towards the stationary phase, the components are separated.

The factors effective on this separation process include molecular characteristics related to adsorption (liquid-solid), partition (liquid-solid), and affinity or differences among their molecular weights. Solutes with different properties are separated based on differences in these interactions. The principle of HPLC are based on VAN DEEMTER EQUTION in which relates the efficiency of the chromatographic column to the particle size of the column /molecular diffusion /thickness of the stationary phase. It has four principles ion exchange, surface adsorption, partion and size exculsion.

Instrumentation of HPLC



HPLC instrumentation is made by typically of six basic components.

1.Solvent delivery system
2.Pumps
3.Sample injection system
4.Columns
5.Detectors
6.Recorders and Intergrators

1.Solvent Delivery System

Resistance to the flow of solvent is high .Such high pressure recommended .The solvents /mobile phase is used must be passed a column at high pressure is about 1000-3000psi,Thepartical size of stationary phase is 5-10M.When solvents pumped in used high pressure, gas bubbles are formed; which will interface with separation process, study base line and shape of peak. They can be done by using vaccum filtration ,helium purging ,ultrasonication.

2.PUMP

The main role of pump is to force the solvent/mobile phase into column .It is placed in upper part of HPLC system and pushes the eluent from solvent reservoir to system column detector. A steady pump pressure is required for reproducibility and accuracy .They are three types;

A .Displacement pumps.
B. Reciprocating pumps.
C. Pneumatic pumps4

3. Sample Injection System

It several devices are available in manual /auto injection of sample, these are three types namely

A. Septum injection
B. Stop flow injection
C. Rheodyne injection

Rheodyne injection is most popular injectors. Injection has two modes ,firstly load position secondly inject mode. Limit of precision of HPLC. Sample size in between 0.5 NM to 500NM. No interference with pressure. Based on sample loop 1~ 100ml, reproductibility 0.1%, pressure <7000psi. It controls the temperature auto sampler inject continuously variable volume 1ml -1ml.5

4.Columns

It is stainless steel tubing for high pressure it is straight 15-150cm, length 2-3mm,The packing material is made up of silica gel, aluminia, celite. It is of three types

A.Analytical column
B. Micro column
C.Guard column

It is used primarily for the separation of proteins and carbohydrates. It removes particular matter and contamination protect, analytical column, similar packing, temperature control<150c,0.1c6

5.Detectors

Detectors used depend upon the property of the compounds to the separated.UV Detector is very commonly used detector for HPLC analysis.The detector senses the presence of the individual components as they leave (elute) the column. It converts change in the effluents into an electrical signal that is recorded by the data system. It is of high sensitivity, good stability and reproduct ability. The temperature rangers from room temperature to atheist 400c. It should be non –destructive [7].

The first industrial metal detectors were developed in 1960s widely used for mining and other industrial purposes. It consists of an oscillator which produces an alternating current that passes through the coil producing alternating magnetic field.

Detectors which allow the selection of the operating wavelength called variable wavelength detectors. Depending on the sophistication of the detector, wavelength change is done manually or programmed on a time basis into the memory of the system. A Detector are two types photon and thermal detectors. All detectors have a similar characteristics, the output of detector must to respond to changes in the incident light intensity. The ability to respond is expressed by quantities such as responsivity, sensitivity and dynamic range [8].

When the radiation passes inside a detector, it causes ionisation of gas atoms, separating atoms into positive ions and electrons. Some detectors are designed to detect antimatter. The detectors are used in HPLC of majorly two types

1. Selective detectors(solute property)
2. Universal detectors (bulk property)

1. Selective Detectors

These detectors respond to a particular physical or chemical property of the solute, being ideally independent of the mobile phase, they as follow;9

1. Absorbance detectors
2. Fluorescence detectors
3. Electro chemical detectors
4. Mass spectro metric detectors

2. Universal Detectors

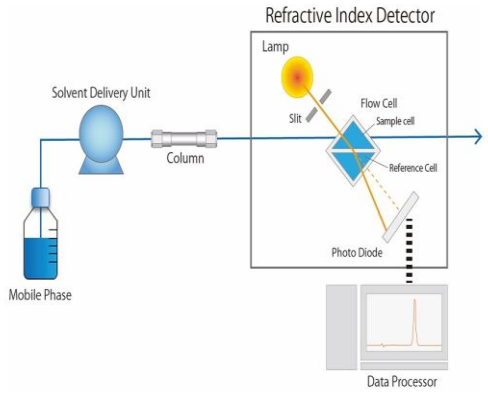
It measures the difference in some physical property of the solute in the mobile phase compare to mobile phase alone. They are generally universal in application but tend to have poor sensitivity and limited range. 10

Detectors Used In Chromatography Techinques

Detectors used depend upon the property of the compounds to be separated. Different detectors available are:

I. Refractive index detectors
II. U.V detectors
III. Fluorescence detectors
IV. Electro chemical detectors
V. Evaporative light scattering detectors
VI. IR detectors
VII. Photo diode array detectors

1. Refractive Index Detectors



Refractive index detectors measures the molecules ability to deflect light in a mobile phase in a flow cell relative to a static mobile phase contained in a reference cell .the amount of detection is proportional to the concentration of the solute in the mobile phase .it is also known as universal detector. An RI detector detects components based on the refraction of light in solution. Prior to analysis , eluate is introduced into either cell, until the flow of the eluate becomes equilibrated [11].

Applications

- It is used with HPLC when detecting substances with limited or no UV absorption.
- It is used for analytes which give no response with other more sensitive and selective detectors.
- It responds to the presence of all solutes in the mobile phase.
- Non ionic compounds monitoring.
- It is used with high pressure liquid chromatography.

- It measures the molecules ability to deflect light in a flow in mobile phase.
- The amount of deflection is proportional to concentration of the solute in the mobile phase.
- It has small linear range only, sensitive to temperature

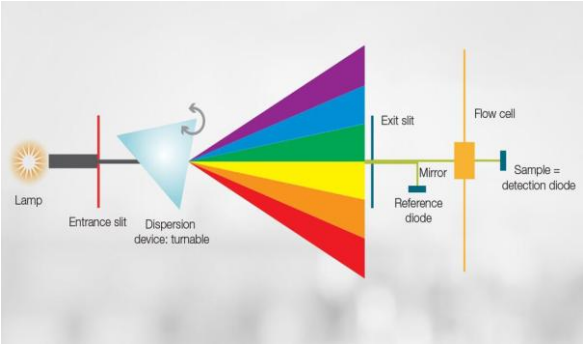
Advantages

- It is of low cost and compatibility with most solvents and columns.
- It passes visible light through two compartments like sample and reference.
- It is of low sensitivity to dirt and air bubbles in the flow cell.
- It has independent of flow rate, universl response.
- It is used for analysis of carbohydrates.
- It is designed for analysis of compounds that do not strongly absorb UV light.

Disadvantages

- It is of high expensive than UV detectors.
- It is highly temperature sensitive.
- It cannot be used with gradient elution and has pressure fluctuations.
- It is affected by the slight changes in mobile phase composition and temperature.
- It is of moderate sensitivity.
- It is of interference from temperature.

2. UV-DETECTORS



It is based on electronic transitions with in molecules. Most common type of detector for LC. Fixed wavelength, Hg lamp 254 nm (π => π*). Tunablewavelength,selectable for specific wavelengths, monochromators or filters.Still limited to single wavelengths. - 1 pgLOD.Solvent limitations with UV-visible detectors.HPLC and UV detectors are used with high performance liquid chromatograph to detect and identify analytes in the sample. UV visible HPLS detector uses light to analyse samples .by measuring the sample absorption of light at different wave length, the analyte can be identified [12].

EX: diode array detector

Applications

- It is used in pharmaceutical and bio pharmaceutical industries.
- It is used in purification of cannabis, hemp, marijuana potency.
- It is used in food and beverages.
- It is used in pet isotope research and production.
- It is used in adhesive, lubricant and detergents.

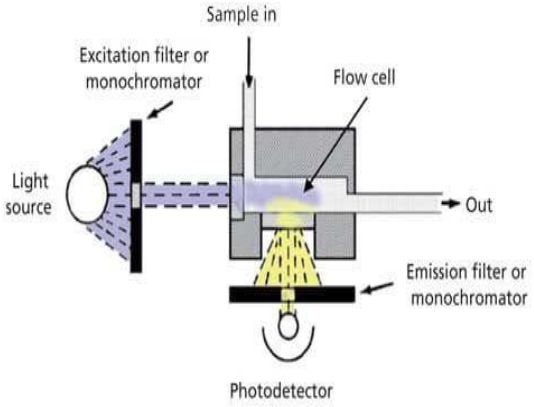
Advantages

- It is easy to use, reliable and have a universal response to chromophoric compounds.
- It has wide availability and compatibility with most solvents and columns.
- It is of low cost, simple design, fast time response , high gain.

Disadvantages

- It is of low sensitivity, limited selectivity.
- It is limited to UV visible absorbing compounds.
- It is time taking process.
- This detector sample using too much wavelength range or by poor instrument design.
- Changing the lamp is a time consuming process.
- It is of expensive instrumentation [13].

3. FLUORESENCE DETECTORS



It is based on emission of excited state molecules.Detector 900 from excitation axis. LOD 10 fg. Hg or Xe lamp.Fluorometer and spectrofluorometer .Fluorescing species or fluorescent derivatives. It extracts the required fluorescence wave lengths and measure the intensity with photo multiplier. HPLC fluorescence (FL) detectors are know for there high sensitivity and specificity over other types of HPLC detectors. FL detectors measure light emission from excited atoms in an analyte in order to obtain information from solution that has been collected from an HPLC column. ex: xenon lamp or LEDs

Appilications

- It is used in analytical detection of presence of proteins.
- It effects of energy from fluorescent groups from each other.
- This method used to demonstrate naturally occurring fluorescent and non fluorescent substances.
- It is changes in fluorescence polarisation to determine shape and size of molecules.
- It is widely used in food, environmental and pharmaceutical fields.

- It is used especially when the analyte has little or no UV absorbance.
- It is used in genetic engineering, DNA analysis.
- Protein conformation, enzymatic reactions are used.
- It is used immune chemical method [14].

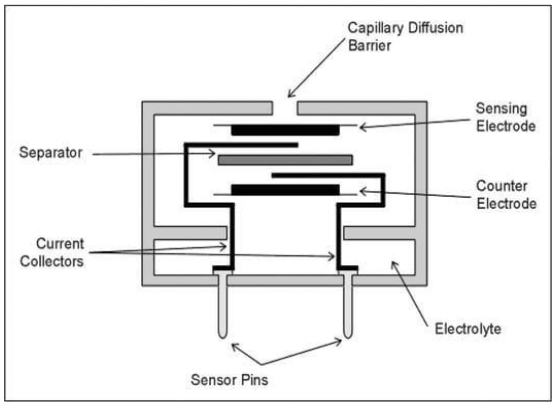
Advantages

- It is of high sensitivity and low back ground noise.
- It can be detected by excitation and fluorescence wave lengths specific to a particular substance.
- It allows detection using small amounts of samples.
- It can be power full tool to increase sensitivity.

Disadvantages

- It is higher in cost, limited availability
- It is difficult to predict fluorescence
- It is not useful for identification of all compounds in fluorescence.
- It has low measurement time.15

4. Electro Chemical Detectors



It is Based on amperometric response of analyte to electrode usually held at constant potential.If the analyte is electro active, can be highly sensitive since response is based on a surface phenomenon rather than a solution bulk property.simplicity, convenience and widespreading application .Thin-layer flow cell of Teflon : 50µm thick, 1 ~ 5 µL volume. Indictor E :Pt, Au, C. Multi -electrode : simultaneous detection or sample purity indication. It is a powerful analytical method that can detect electric currents generated from oxidative or reductive reactions in test compounds.

EX: amperometric electrodes [16].

Applications

- Electrochemical biosensors are avaliable for co and oxygen.
- Biosensors and detectors for pesticides.
- It provides a broad array of quantitative methods for detecting important analytes .
- The level of current is directly proportional to the analyte concentration.
- It includes hospitals, factories and environmental monitoring.
- It detects of the neurotransmitters, environmental assessment.
- The detection of phenol compounds from food sample.
- These techniques have been efficiently used for accessing soil fertility.

Advantages

- It is simple measurement procedure.
- It has sufficient sensitivity and selectivity.
- It is of low cost, non toxic and materials
- It is low detection limits (Nm)
- It has no need for derivation of the analyte prior to analysis.
- It is easily miniaturized for used in capillary LC and CE methods

Disadvantages

- It is of limited temperature range.
- It has limited life span.
- It is of cross –affectability of different gases.
- The electrode response could drift with time.
- It is requiring more frequent calibration with standards.
- It is impact on the global environment [17].

5. Evaporative Light Scattering Detectors

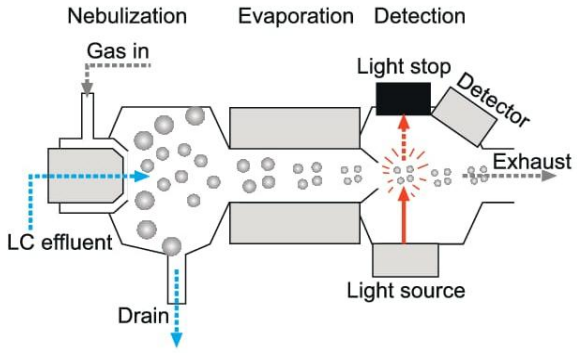


Fig. 1. Evaporative light scattering detector (ELSD).

Responds to any analyte that is significantly less volatile than the mobile phase. Eluate is mixed with N 2(g) and forms a fine mist. Solvent evaporates leaving from the fine particles of analyte. The particles themselves are detected by light scattering. Response is proportional to analyte mass. This detectors suitable for the detections of non volatile sample components in a volatile eluent. These are aerosol-based on HPLC detecors which work by converting the eluents of targent components to a fine spray via a nebulizer. It is also know as evaporative mass detector. This which solve the problems in extremely simple way.

Ex: carbohydrate and natural sugars

Applications

- It is commonly used for carbhodrayte,lipid and polymer analysis.
- It is a universal detector.
- Detection is based on the scattering of a beam light by particles of compound remaningafter evaporation of the mobile phase.

- It is useful for large molecular weight molecules like surfactants,lipids and sugar.
- It is ELSD is an ideal detector for drug discovery, combinatorial chemistry, and the analysis of natural substances.

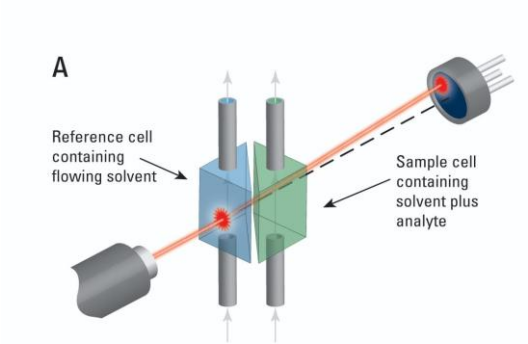
Advantages

- Ideal for high throughput screening and quantification.
- ELSD compatabile with a much wider range of solvents compared to refractive index detector.
- No interference some solvents front peaks.
- It cannot any sample preparation.
- It is not dependent on spectroscopic properties of analyte.
- It is universal-responds to all compounds in the mobile phase.

Disadvantages

- ELSD detector designs has been that high operating temperature required to fully evaporate eluend.
- A binder less process and no physical bonding is required to bind the sand aggregates.
- This can cause loss of semi volatile, small molecules.
- Removal of mobile phase eluent allows rapid HPLC gradients [18].

6.IR Detectors



Filter instrument or FTIR. Similar cell (V, 1.5 ~ 10 µL and b, 0.2 ~ 1.0mm). Limit: no suitable solvent, special optics. FT-IR allows for spectrum records of flowing systems analogous to the diode array system. Water/alcohols can be major interferences to solute detection.LOD 100 ng. when the IR radiation falls on the detector junction, the junction heats up. This causes a difference in temperature between the detector junction and reference junction. This generates a potential difference between this two and is detected by the volte meter. It is also called as pyroelectric detector.

Ex: thermocouple and thermopile

Applications

- It is widely used in motion detectors.
- It is used in building service to switch on lamps or in alarm systems.
- The sensor elements to detect the heat radiation that changes over time and space due to the moment of the people.
- The IR sensor is used for calculating the distance between the sensor and the objects.
- The temperature of detector is used for industrial temperature control.
- Ultrasonic detector is used for distance measurement.
- They can use as gas analyzers.
- They detect radiation thermometers.

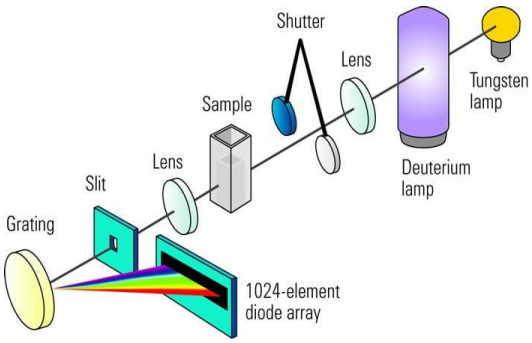
Advantages

- It is low power consumption.
- It is of simple design and useful features.
- IR signals are un detectable to the human eye.
- IR radiation can be found in the visible and micro wave regions.

Disadvantages

- Infrared can be used for a small range distance.
- The speed of data transfer in infrared is slow.
- The transmission data rate is low it is can be affected by environmental conditions.
- The prolonged exposure to IR radiation causes a gradual.
- But it causes a irreversible opacity of the lenses.
- Low level of IR absorption can cause symptoms such as redness of eye, swelling or haemorrhaging.

7. Photo Diode Array Detectors



This is a recent one which is similar to U.V detector which operates from 190- 600 nm. Allows for the recording of the entire spectrum of each solute as it passed through the diode array detector. The resulting spectra is a 3-D or three dimensional plot of Response vs Time vs Wave length.thesedetecors record light absortionat different wave lengths and can provide spectra of the analytes. This useful in identifying unknows, this detects the absorption in UV to visible region. It measures the entire wave length range in real time. It is also known as diode array detector. Ex: linear arrays [19].

Applications

- A PDA detector can monitor a sample at more then one wave length.
- This is especially useful when the wavelength maxima of the analytes.
- Wave length can be selected to analyse in each compound and its highest sensitivity.

- Diode arrays are commonly used for core driver switching, high frequency data lines, LAN and WUAN networks.
- It is used for semi conductor devices.
- It is turning AC to DC isolating signals from a supply, and mixing signals.
- It can be changing AC current to DC current by removing some part of the signal.
- They are used in electrical switches [20].

Advantages

- The potential for measuring multiple wavelengths.
- At once, there by measuring the entire spectrum of species.
- Photo diode arrays are not that sensitive.
- It can operate at high frequencies.
- It can be used as variable resistance device.
- It has better frequency response, linearity and spectral response than LDR [21].

Disadvantages

- Rapid increase dark current and it depends on temperature.
- Small active area.
- Photo diode charactersitics are temperature dependent and have a poor temperature stability.
- It is significantly less sensitive.
- It shows slower response time than other diodes.
- Diodes have high reverse recovery time due to significant power loss [22].

Recorder and Integrators

Recorders are used to record the response obtained from detectors after amplification. They record the base line and all the peaks obtained, with the respect to time. ntegrators are improve version of recorders with some data processing capabilities. These provide more information on peaks then recorder. They can record the individual peaks with retention time, height and width of peaks, % area [23].

Conclusion

It can be concluded from the entire review that HPLC is a versatile, reproducible chromatographic technique for the estimation of drug products. It has wide applications in different fields in term of quantitative and qualitative estimation of active molecules. All the products of degradation formed during the stress conditions and the active pharma ingredient were well separated and peaks were well resolved from each other and separate with an appropriate retention time indicating that the proposed method to be fast, simple, feasible and affordable in assay condition.

This review provides a general overview of HPLC method development and validation. A general and very simple approach to developing HPLC methods for compound separation was discussed. Developed and validated RP-HPLC for Remdesivir were found to be simple, rapid, specific, sensitive, precise and cost effective. This analytical method can also be applied for assay and related substances stability testing studies for the respective drug.

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Conflict of Interest

No Conflict of Interest

Inform Consent and Ethical Considerations

Not Applicable

Author Contribution

All authors are contributed equally.

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