

Study of Addictive Medicines and HPLC Method

Jyoti Yadav

Mahendergarh, Haryana, India.



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Abstract

The addiction medicine is a medical specialty that deals with the treatment of addiction. The specialty often crosses over into other areas, since various aspects of addiction fall within the fields of public health, psychology, social work, mental health counseling, psychiatry, and internal medicine, among others. Incorporated within the specialty are the processes of detoxification, rehabilitation, harm reduction, abstinence-based treatment, individual and group therapies, oversight of halfway houses, treatment of withdrawal-related symptoms, acute intervention, and long term therapies designed to reduce likelihood of relapse.

Introduction

Some specialists, primarily those who also have expertise in family medicine or internal medicine, also provide treatment for disease states commonly associated with substance use, such as hepatitis and HIV infection. Physicians specializing in the field are in general agreement concerning applicability of treatment to those with addiction to drugs, such as alcohol and heroin, and often also to gambling, which has similar characteristics and has been well-described in the scientific literature.

There is less agreement concerning definition or treatment of other so-called addictive behavior such as sexual addiction and internet addiction, such behaviors not being marked generally by physiologic tolerance or withdrawal.

Doctors focusing on addiction medicine are medical specialists who focus on addictive disease and have had special study and training focusing on the prevention and treatment of such diseases. There are two routes to specialization in the addiction field: one via a psychiatric pathway and one via other fields of medicine.

The American Society of Addiction Medicine notes that approximately 40% of its members are psychiatrists (MD/DO) while the remainder has received primary medical training in other fields.

Concept of Drugs

The World Health Organization (WHO) defines drug as any substance which, introduced into the living organism can modify one or more of its functions.

The presence of drugs in many civilizations goes back to time immemorial. Greeks and Romans deified wine with the figures of Dionysus and Bacchus, respectively. Historically, drugs have been linked to magical-religious rituals, celebrations and social events. Gradually their use became widespread in other

contexts. Some of these substances are natural in origin, as is the case with tobacco or cannabis. Others are the result of chemical processes carried out using natural products, like what occurs with alcoholic beverages, which are obtained from the fermentation or distillation of grain or fruit juice. Drugs are also produced artificially. This is the case for drugs for psychiatric use or for synthetic drugs.

Need of Drug Analysis

The number of drugs introduced into the market is increasing every year. These drugs may be new entities or existing partial structural modifications. From the date the drug enters the market, there will usually be a period of delay until the drug enters the Pharmacopoeia.

This is because the continued and widespread use of these drugs may have uncertainties, report new toxicities (causing them to exit the market), long standing opposition developments and the introduction of better drugs by competitors. Under these conditions, the standard and analytical procedures for these drugs may not be available for pharmacopoeia. Therefore, it is necessary to develop new analytical methods for such drugs.

Quality is important for every product or service, but it is critical for life-related drugs. Quality control is a concept that aims to produce a perfect product through a series of measures designed to prevent and eliminate errors at different stages of production.

The decision to issue or reject a product is based on one or more control actions. With the development of the pharmaceutical industry in recent years, the rapid development of the field of drug analysis for complex instruments, providing a simple analytical procedure for complex formulations is the most important issue.

In short, the reason for developing an updated drug analysis method is that the drug or combination of drugs may not be official in any pharmacopoeia.

Due to limitations of patent regulations, the appropriate drug analysis procedures may not be available in the literature. The Analytical methods may not be used for the formulation of drugs due to interference caused by the formulation excipients; analytical methods for drug quantitation in biological fluids may not be available.

Analytical methods that combine technetium with other drugs may not be available for Existing analytical procedures may require expensive reagents and solvents. It may also involve cumbersome extraction and separation procedures, which may not be reliable.

Chromatographic Methods

The modern pharmaceutical formulations are complex mixtures containing one or more therapeutically active ingredients, for a number of inert materials such as excipients, disintegrates, color and flavor.

In the order to ensure that the quality and stability of the final product, pharmaceutical companies, and the analyst must be able to separate the mixture into individual components for quantitative analysis.

The Chromatography is a powerful technology that enables the differential between the components in

two stages, one of which is known as the stationary phase and the other one is movable, is a moving stage. The sample species have been repeated interactions (partition) between mobile and stationary phase by phase.

The Stationary phase may be solid or liquid (supporting a solid or gel) and packed in a column, expanded to a layer or film. The mobile phase may be gaseous or liquid. These solutes, distributed priority in the mobile phase, and will quickly through the system, the distributed priority phasing. This forms the basis of the split components.

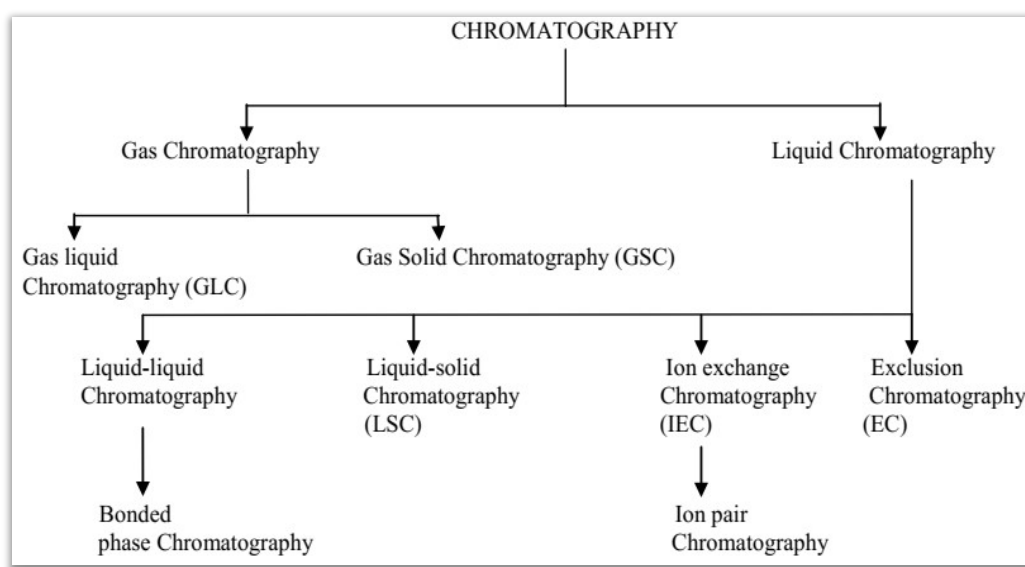
A solute between the two phases, from the balance of forces between the solute molecules and elements of each phase. It reflects the relative attractiveness, or repulsion molecule or ion the competitive phase, the solute and them. These units can be used in the polarity of the induced and permanent dipole moments. In the ion exchange chromatography, the forces in the solute molecules will go a long way in the ionic nature, including polar and non-polar forces.

Chromatography Method must have in essence:

- Stationary phase
- Mobile phase
- Sample injection system
- Solvent delivery system
- Column phase
- Detection by detecting agent

All chromatographic methods involve modifications in these basic components

Figure 1.1: Showing Classifications of Chromatographic Methods



The Chromatographic methods can be classified according to the nature of the stationary and mobile phases.

Different types of chromatography are:

- Adsorption chromatography
- Partition chromatography
- Ion exchange chromatography
- Size exclusion or gel permeation chromatography.

Modern instrumental techniques of GLC and HPLC provide excellent separation and allow accurate assay of very low concentrations of wide variety of substance in complex mixtures.

High Performance Liquid Chromatography (HPLC)

This is a sophistication of the century-old technique and is the most widely used of all the analytical separation techniques. In high performance liquid chromatography (HPLC) the liquid mobile phase is forced through the stationary phase under pressure. A simple HPLC includes a solvent reservoir to hold the mobile phase, a pump to pressurize the mobile phase, and injector to allow injection of a small volume of the sample mixture under high pressure, a column containing the bed of stationary phase, a detector to detect the presence of components as they exit the column, and a recorder to record the detector signal.

Most of the drugs in dosage forms can be analyzed by HPLC technique because of the several advantages like rapidity, specificity, accuracy, precision and ease of automation in this method. HPLC method eliminates tedious extraction and isolation procedures. Some of the advantages are:

- Speed (analysis can be accomplished in 20 minutes or less)
- Greater sensitivity (various detectors can be employed)
- Improved resolution (wide variety of stationary phases)
- Reusable columns (expensive columns but can be used for many analysis)
- Ideal for the substances of low volatility
- Easy sample recovery, handling and maintenance
- Instrumentation tends itself to automation and quantitation (less time and less labor)
- Precise and reproducible
- Calculations are done by integrator itself
- Suitable for preparative liquid chromatography on a much larger scale

There are different modes of separation in HPLC. They are normal phase mode, reversed phase mode, reverse phase ion pair chromatography, affinity chromatography and size exclusion chromatography (gel permeation and gel filtration chromatography).

Normal Phase Mode

In the normal phase mode, the stationary phase is polar and the mobile phase is nonpolar in nature. In this technique, nonpolar compounds travel faster and are eluted first. This is because of the lower affinity between the nonpolar compounds and the stationary phase.

Polar compounds are retained for longer times because of their higher affinity with the stationary phase. These compounds, therefore take more times to elute.

Normal phase mode of separation is therefore, not generally used for pharmaceutical applications

because most of the drug molecules are polar in nature and hence take longer time to elute.

Reversed Phase Mode

Reversed phase mode is the most popular mode for analytical and preparative separations of compound of interest in chemical, biological, pharmaceutical, food and biomedical sciences.

In this mode, the stationary phase is nonpolar hydrophobic packing with octyl or octadecyl functional group bonded to silica gel and the mobile phase is polar solvent. An aqueous mobile phase allows the use of secondary solute chemical equilibrium (such as ionization control, ion suppression, ion pairing and complexation) to control retention and selectivity.

The polar compound gets eluted first in this mode and nonpolar compounds are retained for longer time. As most of the drugs and pharmaceuticals are polar in nature, they are not retained for longer times and hence elute faster.

The different columns used are octa decyl silane (ODS) or C18, C8, C4, etc., (in the order of increasing polarity of the stationary phase).

Ion Exchange Chromatography

In ion exchange chromatography, the stationary phase contains ionic groups like NR_3^+ or SO_3^- , which interact with the ionic groups of the sample molecules. This is suitable for the separation of charged molecules only. Changing the pH and salt concentration can modulate the retention.

Ion Pair Chromatography

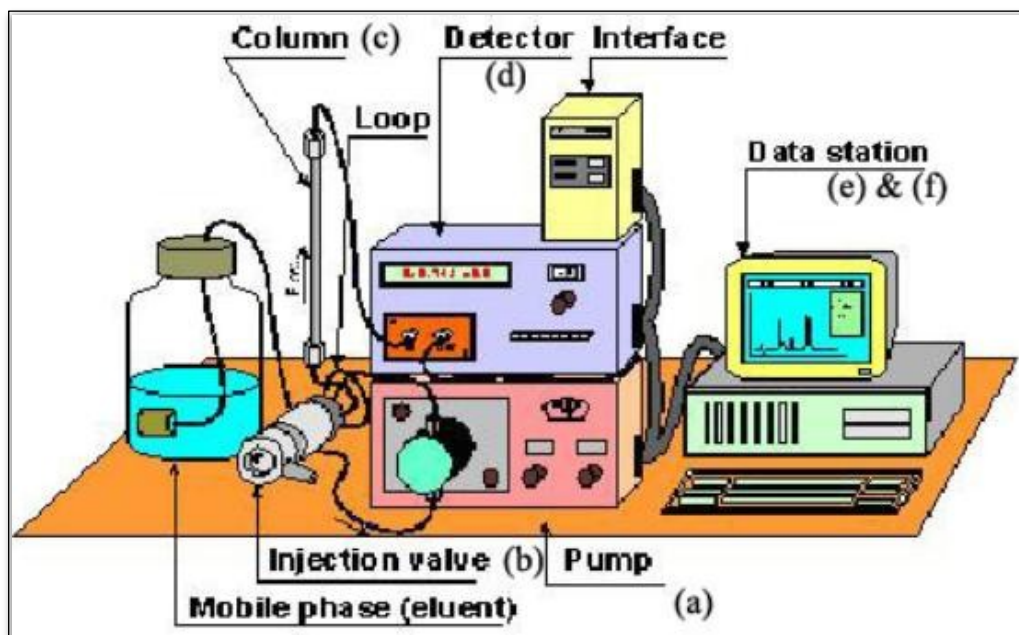
Ion pair chromatography may be used for the separation of ionic compounds and this method can also substitute for ion exchange chromatography. Strong acidic and basic compounds may be separated by reversed phase mode by forming ion pairs (columbic association species formed between two ions of opposite electric charge) with suitable counter ions. This technique is referred to as reversed phase ion pair chromatography or soap chromatography.

Affinity Chromatography

Affinity chromatography uses highly specific biochemical interactions for separation. The stationary phase contains specific groups of molecules which can absorb the sample if certain steric and charge related conditions are satisfied. This technique can be used to isolate proteins, enzymes as well as antibodies from complex mixtures.

Size Exclusion Chromatography

Size exclusion chromatography separates molecules according to their molecular mass. Largest molecules are eluted first and the smallest molecules last. This method is generally used when a mixture contains compounds with a molecular mass difference of at least 10%. This mode can be further subdivided into gel permeation chromatography (with organic solvents) and gel filtration chromatography (with aqueous solvents).

Figure 1.2: Showing a Schematic Diagram of HPLC Equipment

Various Components of HPLC are as following:

- (a) A solvent delivery system, including pump,
- (b) A sample injection system,
- (c) A chromatographic column,
- (d) A detector,
- (e) A strip chart recorder,
- (f) A data handling device and microprocessor control.

Solvent Delivery System

A mobile phase is pumped under pressure from one or several reservoir and flows through the column at a constant rate. For normal phase separation-eluting power increases with increasing polarity of the solvent but for reversed phase separation, eluting power decreases with increasing polarity.

A degasser is needed to remove dissolved air and other gases from the solvent. Special grades of solvents are available for HPLC and these have been purified carefully in order to remove absorbing impurities and particulate matter to prevent these particles from damaging the pumping or injection system or clogging the column.

Pump

The pump is one of the most important components of HPLC, since its performance directly affects retention time, reproducibility and detector sensitivity. Three main types of pumps are used in HPLC to propel the liquid mobile phase through the system. These are given below:

Displacement Pump

It produces a flow that tends to independent of viscosity and backpressure and also output is pulse free. But it possesses limited capacity (250 ml).

Reciprocating Pump

It has small internal volume (35 to 400 μl), their high output pressure (up to 10,000 psi) and their constant flow rates, but it produces a pulsed flow.

Pneumatic or Constant Pressure Pump

They are pulse free; suffer from limited capacity as well as a dependence of flow rate on solvent viscosity and column backpressure. They are limited to pressure less than 2000 psi.

Sample Injection System

Insertion of the sample onto the pressurized column must be as a narrow plug so that the peak broadening attributable to this step is negligible. The injection system itself should have no dead (void) volume. There are three important ways of introducing the sample into injection port:

Loop Injection: In which, a fixed amount of volume is introduced by making use of fixed volume loop injector.

Valve Injection: In which, a variable volume is introduced by making use of an injection valve.

On Column Injection: In which, a variable volume is introduced by means of a syringe through a septum.

Chromatographic Column

The column is usually made up of heavy glass or stainless steel tubing to withstand high pressure. The columns are usually 10-30 cm long and 4-10 mm inside diameter containing stationary phase at particle diameter of 25 μm or less. Columns with an internal diameter of 5 mm give good results because of compromise between efficiency, sample capacity, and the amount of packing and solvent required.

Column Packing

The packing used in modern HPLC consists of small, rigid particles having a narrow particle size distribution. There are three main types of column packing in HPLC.

Porous, Polymeric Beds

Porous, polymeric beds based on styrene divinyl benzene co-polymers used in ion exchange and size exclusion chromatography. For analytical purpose these have now been replaced by silica based, packing which are more efficient and more stable.

Porous Layer Beds

Consisting of a thin shell (1-3 μm) of silica or modified silica on a spherical inert core (e.g. Glass). After the development of totally porous micro particulate packing, these have not been used in HPLC.

Totally Porous Silica Particles (dia. < 10 μm)

These packing have widely been used for analytical HPLC in recent years. Particles of diameter > 20 μm are usually dry packed, while particles of diameter < 20 μm are slurry packed in which particles are suspended on a suitable solvent and the slurry so obtained is driven into the column under pressure.

Detectors

The function of the detector in HPLC is to monitor the mobile phase as it merges from the column. Detectors are usually of two types:

Bulk Property Detectors

It compares overall changes in a physical property of the mobile phase with and without an eluting solute. e.g. refractive index, dielectric constant or density.

Solute Property Detectors

It responds to a physical property of the solute, which is not exhibited by the pure mobile phase ^[18], e.g. UV absorbance, fluorescence or diffusion current. Such detectors are about 1000 times more sensitive giving a detectable signal for a few nanograms of sample.

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