A Review on Frequency of Analytical Techniques Recommended by BP for Specific Formulations

By

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Bachelor of Pharmacy (Hons.)

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Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing a degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

The project titled “A review on frequency of analytical techniques recommended by BP for specific formulations” submitted byAfroza Akter Samia (19146024) of Spring 2019 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of pharmacy on April, 2023.

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Ethics Statement

The project does not involve any clinical trial or human participants, no animals were used or harmed.

Abstract

This study was conducted to develop a database of 209 formulations by identifying dosage form and categorizing assay types and subtypes of each formulation from 1247 specific formulation monographs present in British Pharmacopoeia.The database showed that Chromatographic techniques are the most common among all the assay types recommended by BP. After chromatography, titrimetric and spectroscopic techniques come respectively as the most recommended methods in drug analysis. The purpose of this study was to provide educational benefits by preparing a database. The database would be useful for students and analytical method developers.

Keywords: British Pharmacopoeia, Assay, Monograph

Dedication

Dedicated to my faculty members, family and friends

Acknowledgement

First of all, I would like to express my gratitude towards Allah for allowing me to complete my thesis paper properly and giving me strength to continue work.

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List of Acronyms

BP	British Pharmacopoeia
USP	United State Pharmacopoeia
Ph.Eur	European Pharmacopoeia
HPLC	High Performance Liquid Chromatography
RP-HPLC	Reversed Phase High Performance Liquid Chromatography
NP-HPLC	Normal Phase High Performance Liquid Chromatography
UV	Ultra Violet
GC	Gas Chromatography
MHRA	Medicines and health care Product Regulatory Agency
IEC	Ion Exchange Chromatography
TLC	Thin Layer Chromatography

Chapter 1Introduction

1.1 Background

Different pharmaceutical dosage forms are developed for improving the health of the people and for the treatment of the disease. They are intended to provide exact therapeutic beneficials required for intended health improvement. To serve this purpose, pharmaceutical formulations must be free from impurities and should contain the required amount for therapeutic effect. Thereby, estimation of the quantity of the drug in pharmaceutical formulations is indeed an important step (Siddiqui, 2017). Different analytical methods are used for assessing the drug quantity.

Spectrometry is a quantitative approach which is used to measure the absorbed or transmitted characteristics of a substance by measuring the intensity of the light passing through it. This analytical method is used to determine the amount of known substance by measuring the frequencies of light (wavelengths) absorbed or transmitted by that particular substance. Spectrometers are used for the detailed measurement of the wavelengths of light absorbed or transmitted and spectrophotometer is used for relative intensity of light. A wide range of applications for quantitative purposes can be seen in physics, biochemistry, pharmaceuticals, agriculture etc.(Renjini & Dileep, 2017). Uv-vis spectroscopy is a technique in which the light absorbed is of different wavelengths in the visible and ultraviolet region of the electromagnetic spectrum. The absorbance of light depends on the nature of the substance. Because of that, each substance produces a unique or specific spectrum which is used for the identification or quantification purpose(A. De Caro, 2015). Atomic spectroscopy is another analytical method

used for the quantification of drug samples. In atomic absorption spectroscopy, the light that is absorbed by the atom is quantified to determine the amount of sample. A specific number of electrons surrounds the nucleus of an element. When an atom is in its most stable orbital configuration, it is known as ground state. After energy is provided, the atom achieves a less stable configuration known as excited state by absorbing it. A specialized light source is used as a source of energy. A flame is utilized for the conversion of the sample into atomic vapor which then absorbs light from the main source of light.In atomic emission spectroscopy, the flame is utilized for the conversion of the sample into atomic vapor and a thermal environment is provided to create excited state atoms. As the excited state is not stable, it causes the atoms to immediately come back to the ground state to achieve less stable configuration by emitting light energy. The emitted light's intensity is used for the identification of a particular element(Bobroff & Hillan, 2017).

Chromatography is an analytical technique which is used to separate a mixture of molecules by applying them onto the surface of a stationary phase (solid, or liquid). Separation occurs when the mixture of molecules moves with the help of a mobile phase through the stationary phase depending on factors such as adsorption, affinity or partition etc. Chromatographic procedures can be categorized into two types. Liquid and gas chromatography(Coskun, 2016). HPLC is one of the most significant methods in analytical methodology and has been utilized for more than 50 % cases(Misiuk, 2010). Structural and functional analysis and purification can be performed using this technique. In HPLC, the mobile phase is passed through the column using high pressure (10-400 atmospheric pressure)(Coskun, 2016). In Normal Phase HPLC technique, the stationary phase is polar and mobile phase is non-polar and separation occurs on the basis of polarity. The polar stationary phase retains the polar component of the analyte. The more polar

the analyte component, the more the adsorption strength. The elution time also gets higher(Patel, 2009). In reverse phase HPLC technique, the stationary phase is nonpolar and the mobile phase and the mobile phase is moderately polar. The principle of reverse phase HPLC is based on hydrophobic interaction. The repulsive forces between polar eluent, non-polar analyte and non-polar stationary phase works behind it(Patel, 2009).Gas chromatography is another chromatographic technique which is utilized for the separation and analysis of gaseous and volatile compounds. In order to separate the components of an analyte, a solvent is used to dissolve the sample which is then vaporized. There are two phases, a stationary phase and a mobile phase and between these two the analyte is distributed. The stationary phase is a column which is either a solid adsorbent or contains liquid coated on an inert solid support. Depending on the type of stationary phase, gas chromatography is either gas liquid chromatography (GLC) or gas solid chromatography (GSC)(Kaur & Sharma, 2018). Chemically inert gasses such as He or N_2 are utilized as mobile phase. The analyte containing a mixture of components is passed through the heated column by the mobile phase (Coskun, 2016). In GSC the separation of components occurs through the absorption process and in GLC the separation occurs through partition(Kaur & Sharma, 2018). In ion exchange chromatography, the sample components are separated depending on the electrostatic interaction which occurs between charged protein groups and supporting material (matrix). The proteins that need to be separated have an opposite charge to the ions loaded in the matrix. The protein gets separated according to the affinity of the proteins to the column ions. By changing ion salt concentration, PH or ionic strength of the buffer solution the proteins are separated from the column (Coskun, 2016). Another chromatographic technique is thin layer chromatography which is based on solid-liquid adsorption. Coating of a solid adsorbent material on a glass plate is called the stationary phase.

The mobile phase along with a solvent moves in the upward direction across the stationary phase because of capillary action. The separation occurs because of varying flow rate of the component of the mixture when it moves by capillary action (Coskun, 2016).

Titrimetry is a volumetric method useful for concentration determination of drug samples for purity assessment. This method involves adding a solution having known concentration to a sample solution with which it reacts quantitatively(Qarah & El-Maaiden, 2023). The added solution with known concentration is called the titrant and the sample solution is called the titrand(GREENFIELD & CLIFT, 1975). The titrant to be added is kept in a burette and is slowly introduced to the analyte and indicator mixture (Sharma et al., 2022). After the reaction is complete, either color change, complex formation or precipitate formation occurs at the equivalent point which is determined by a chemical reagent called indicator(Qarah & El-Maaiden, 2023). Acid-base titrations are used for the analysis of drugs which can be categorized as acid or bases by their functional groups. This type of titration simply involves titration of acid/bases with consequent acid/base(Qarah & El-Maaiden, 2023). During this type of titration the pH or relative concentration of the acid or base needs to be monitored (Sharma et al., 2022). H_2O is formed after reaction of H^+ with OH^- in this titration(Qarah & El-Maaiden, 2023). Litmus paper is one indicator in acid-base titration. In acidic solution the litmus paper is red and in basic solution the litmus paper is blue. In aqueous acid-base titration the analyte is being made by dissolving the drug substance into a solution containing water (Sharma et al., 2022). In non-aqueous titration, the sample is titrated without the presence of water. Non-aqueous titrants are utilized for this(Qarah & El-Maaiden, 2023). Weak acids or bases are titrated using this analytical technique by dissolving them into acidic or basic solutions to convert them as strong acids or bases respectively. Different non-aqueous indicator solutions such as Oracet blue B,

crystal violet are used to indicate the end point of the titration(Sharma et al., 2022). Complexometric titration involves complexation reactions where complexing agents are used. EDTA (ethylenediaminetetraacetic acid) is a complexing reagent which is used to combine ions to form complexes in this type of reactions. Metal ion indicators are used to determine the end point (Qarah & El-Maaiden, 2023). Redox titrations have wide use in pharmaceutical analysis among other titrimetric methods. This type of titration is carried out using oxidizing and reducing agents. In a redox reaction, the one which oxidizes others by accepting electrons from them is the oxidizing agent and the one which causes reduction by losing electrons is the reducing agent. In order to complete a redox reaction accompanied by a sharp end point, there should be enough difference between the reducing and oxidizing capabilities of these agents. When the equivalence point is close to achieve, an indicator with oxidation or reducing capability causes an instant change in the electrode potential (Marie, 2015). Precipitate formation is the basis of precipitation titration. As the analyte and titrant react with each other, an insoluble precipitate is formed which is used to determine the end point of this reaction. The most common titrant in precipitation reaction is Ag^+ and analyte is Cl^- and SCN^-. Drugs that are present as chloride salt are mainly assayed in analytical chemistry(Qarah & El-Maaiden, 2023).

Gravimetric method is a quantitative method where the weight of a pure compound is determined which is chemically related to the analyte.The measured weight is used for the calculation of mass percentage of the analyte in the sample. Gravimetric analysis provides more accuracy in comparison to other analytical methods as weight measurement can be done more precisely than other properties. But the process is lengthy and time consuming so it has no wide use. Different types of Gravimetric analysis are: Volatilization Gravimetry, Precipitation Gravimetry, Particulate Gravimetry and Electrogravimetry (Saeed, 2019).

In immunological techniques, the amount of analyte (antigen) is quantified based on the reaction between antigen and antibody. In order to bind to a small number of binding sites on a highly specific anti-analyte antibody, a competitive binding interaction occurs between a particular amount of an analyte which is labeled and an unlabeled sample of variable amount which forms the basis of this technique. This technique has a wide range of use in therapeutic drug monitoring, disease diagnosis and pharmaceutical industries (Darwish, 2006).

The British pharmacopoeia is the United Kingdom's national pharmacopoeia. Under the medicine act of 1968, BP and BP commission was established legally but it has been responsible for providing standards since 1864. The national authority responsible for the quality specifications and standard of medicines used in that United Kingdom prepared a legally combined collection having details about drug making which is termed as pharmacopoeia(World Health Organization (WHO), 2013). British pharmacopoeia represents the pharmaceutical standards of the UK and works as a guideline for specification tests and licensing of medicines and medicinal products regulated by MHRA.

The British pharmacopoeia is a broad compilation containing standards and quality requirements of medications used in a particular area or country. National or regional authority is usually responsible for preparing it. A set of relevant tests to ensure the purity, quality of the drug product and the strength of active ingredients are termed as quality specifications. The stated standards and quality specifications are significant for the adequate functioning or proper control of the regulatory authorities in terms of handling medicines (World Health Organization (WHO), 2013). BP is a trusted reference used by organizations and personnel assigned in research, production, quality control etc. It has a global reach across 100 countries and serves as an expert advisory body to other pharmacopoeias and World health organizations. It plays a significant

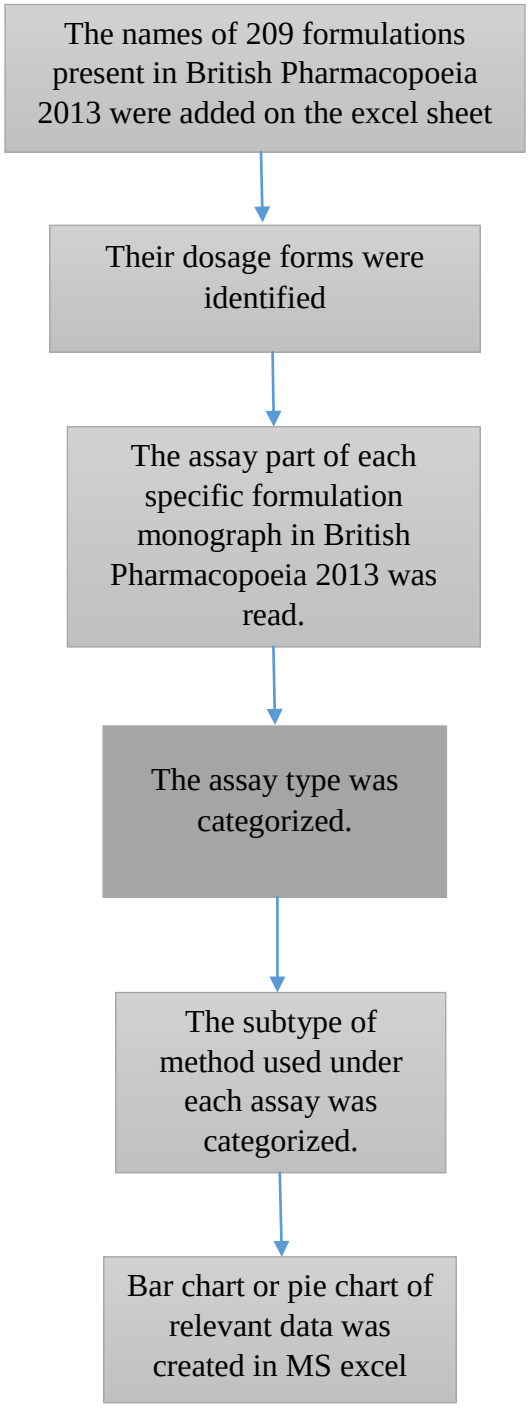
part of the established pharmaceutical legislation in commonwealth nations. The general and specific monographs included in BP are prepared by incorporating with the expert advisory group (EAG) of BP commission, BP laboratory, other pharmacopoeias etc. Several steps are involved in monograph development and are reviewed time and again by EAG and changes are made accordingly. BP laboratory ensures British pharmacopoeia's reliability by performing practical evaluation of analytical procedures and by giving scientific opinion to the BPC. The BPCRS (British Pharmacopoeia Chemical Reference Substances) are procured, maintained and prepared by BP laboratory. The reviewed standards and scientifically evaluated quality specifications makes BP as a reference tool across the globe. (Home - BritishPharmacopoeia, n.d.)

1.2 Aim and Objective

The aim of this study was to develop a database for educational purposes having information about the dosage form, the type and subtype of assay techniques used for the quantification of drug formulations present in British Pharmacopoeia 2013. The objective was to analyze the database and find out which type of assay technique is more frequently used in pharmaceutical analysis. The database also indicated the frequently used subtypes of each assay type for estimation of drug quantity adopted by British Pharmacopoeia. No such study was conducted before and it will help students to understand the frequently used assay types in pharmaceutical analysis and to analyze the purpose behind selecting it.

Chapter 2 Method

The following method was used for conducting the study.



Chapter 3 Result & Discussion

The obtained database is shown in the appendix.

3.1 Categorization

The assay was categorized into chromatographic, spectroscopic, titrimetric, immunological, gravimetric etc. each category was further classified into following types:

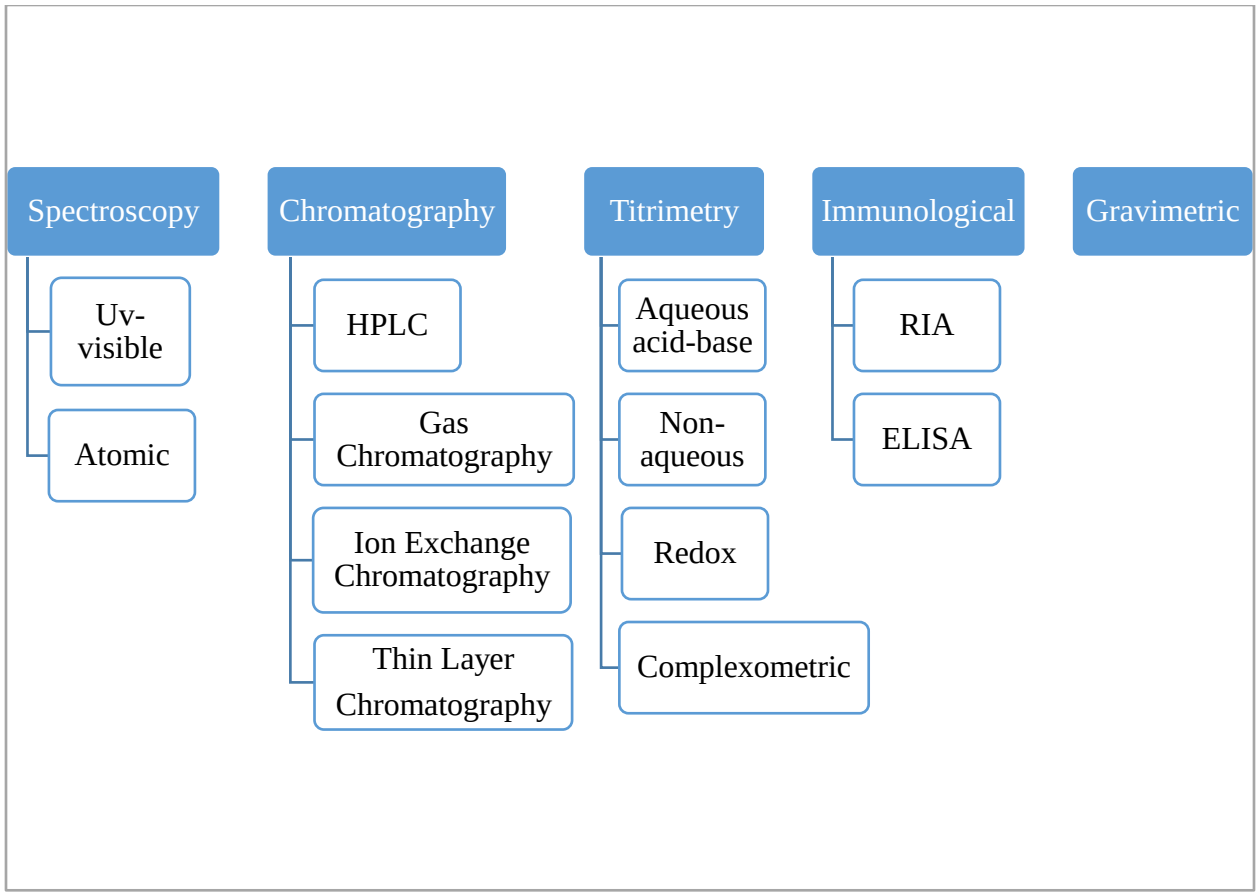


Figure 1: Categorization of Assay Methods

The frequency of assay type used in the quantification of drugs under BP 2013 is shown by the following Charts.

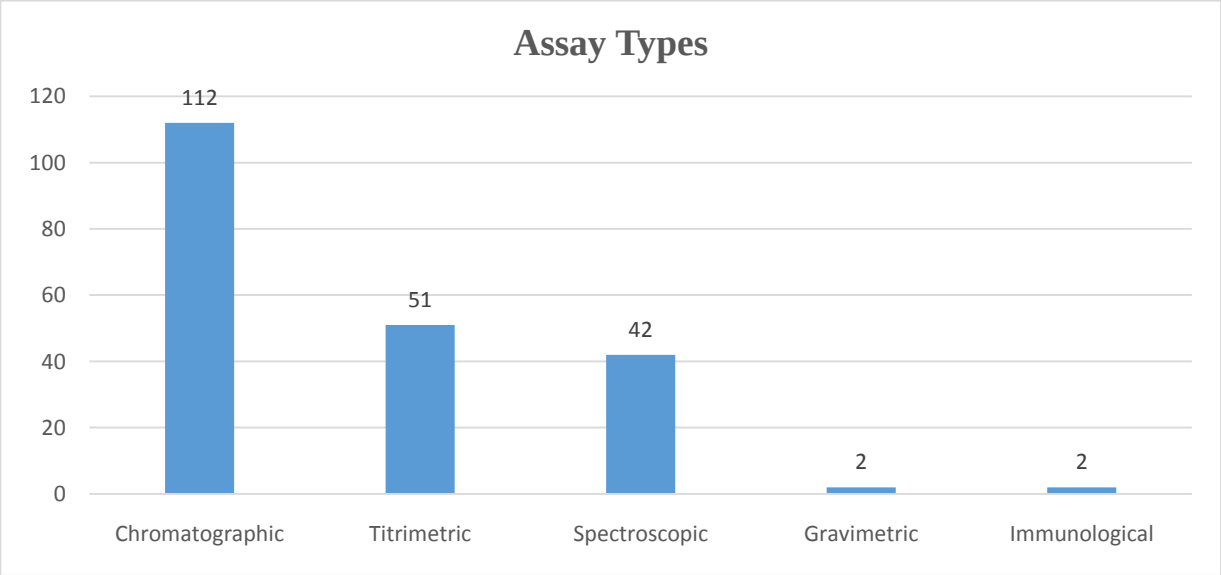


Figure 2: Bar Chart Showing Frequency of All Assay Types

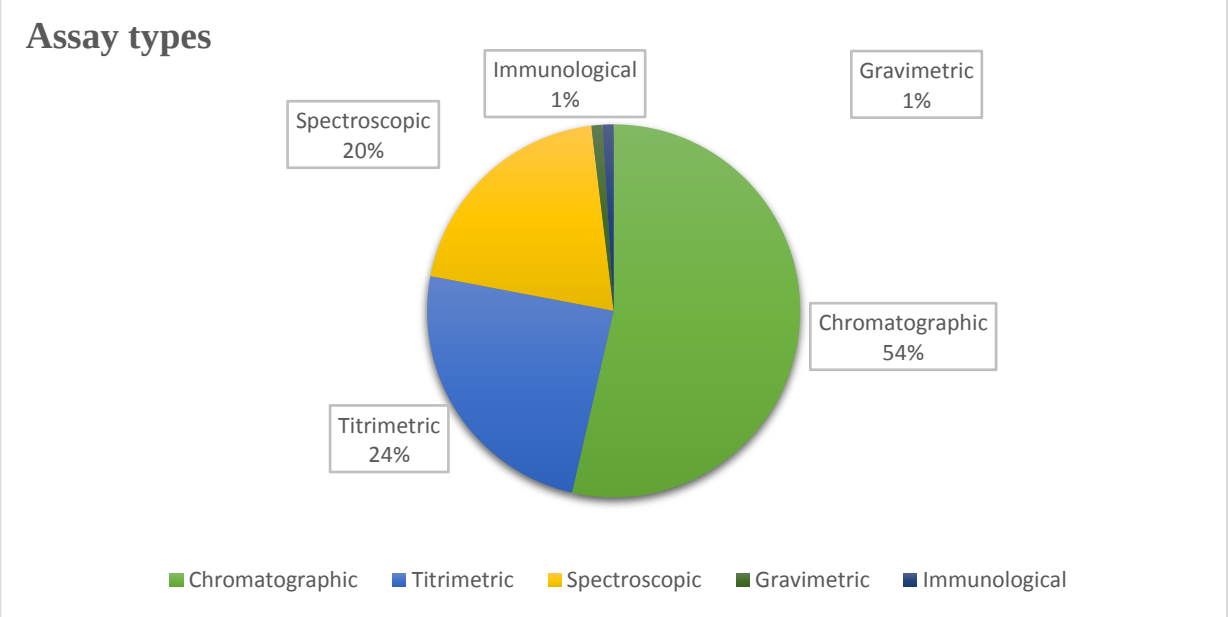


Figure 3: Pie ChartShowingFrequency of All Assay Types

For the formulations studied, 54% were recommended by the BP to be assayed by chromatography. Spectroscopic and titrimetric assays were common. Immunological and gravimetric assays were least recommended.

3.2 Chromatographic Assays

The following pie chart shows how frequently each sub type of chromatographic techniques are recommended.

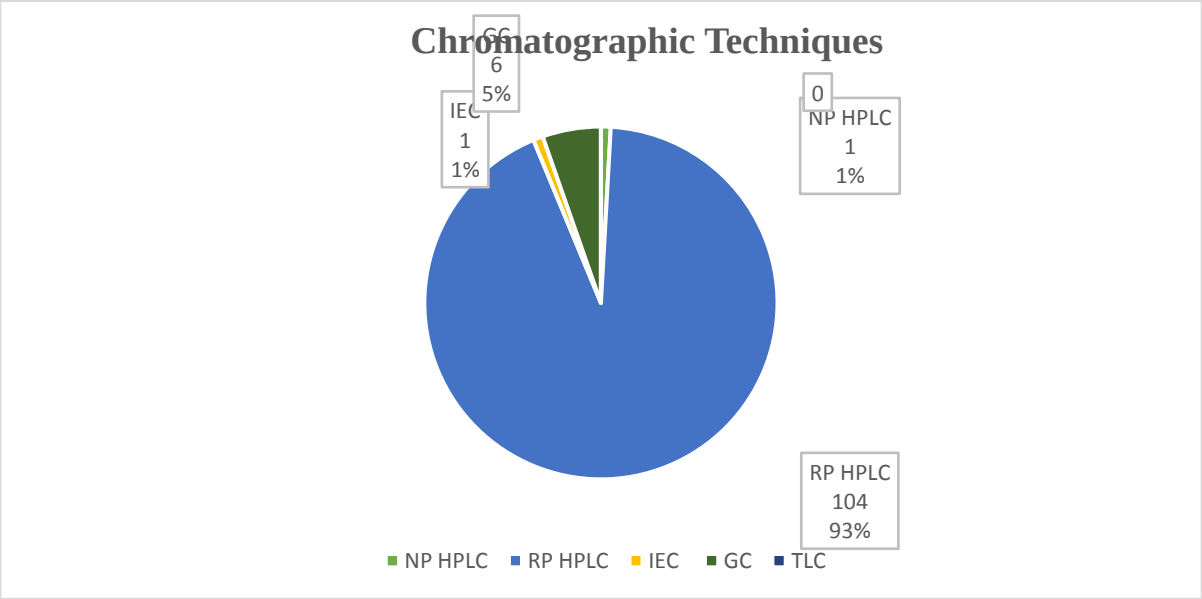


Figure 4: Pie Chart Showing Frequency of Chromatographic Techniques

Out of 112 chromatographic assays studied, 104 were RP-HPLC assays. GC was recommended 6 times.

HPLC has the highest percentage among other chromatographic techniques because of its specificity, accuracy and precision. Compounds having a diverse range of polarity can be analyzed using this technique. Approximately 45% of monographs present in 29th United states

Pharmacopoeia has HPLC as an assay technique of their drug products (Misiuk, 2010). Same goes for our study as HPLC is the most prevalent among other chromatographic techniques. RP-HPLC is mostly used as most of the drugs are organic compounds. After HPLC, GC is another most used chromatographic technique for drug analysis where the drug compound is thermally stable and volatile. It has been replaced a lot by HPLC lately as HPLC provides high precision and suitability for thermally unstable and high molecular weight compounds. NP HPLC and IEC are the least used in comparison to other chromatographic techniques.

3.3 Spectroscopic Assays

The following pie chart shows how frequently each sub type of spectroscopic techniques are used:

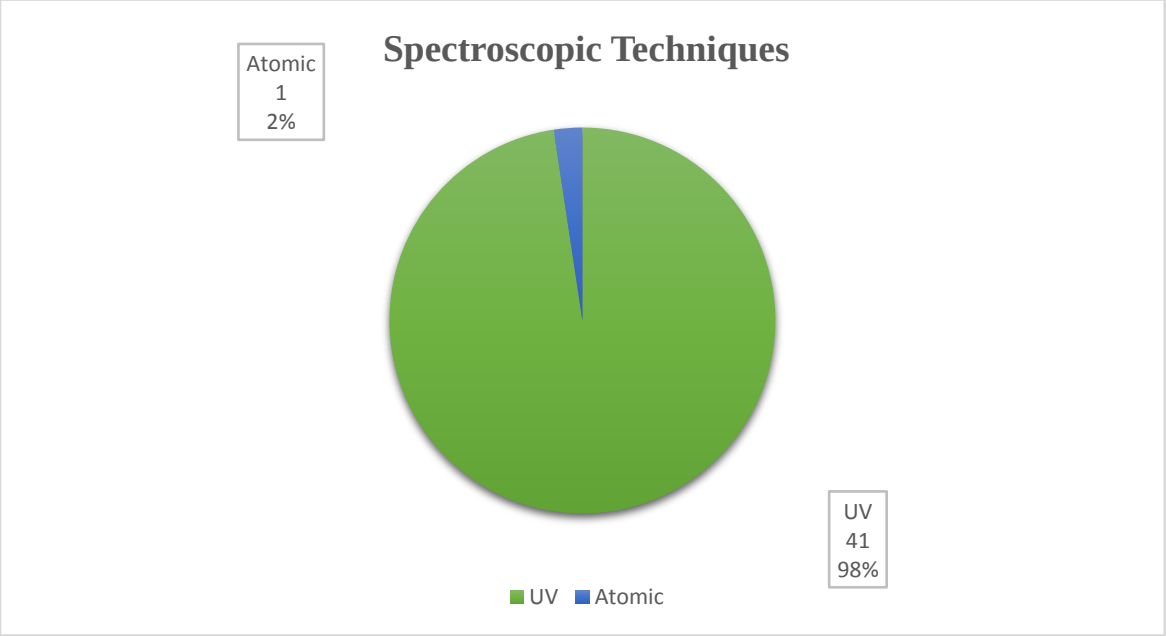


Figure 5: Pie Chart Showing Frequency of Spectroscopic Techniques

Almost all spectroscopic assays utilized UV-visible spectroscopy.

The acquired database shows the third most abundant use of spectroscopy as a technique in drug analysis. Uv-visible spectroscopy has most prominent use among other spectroscopic techniques because of its accuracy, finest detection sensitivity and reproducibility in analysis of drugs. The latest version of USP-36, NF31 contains more than 200 specific monographs that includes UV-visible spectroscopic measurement (Qarah & El-Maaiden, 2023).The importance of atomic spectroscopy is increasing with time because of its sensitivity and selectivity but still has no wide use.

3.4 Titrimetric Assays

The following pie chart shows how frequently each sub type of titrimetric techniques are used:

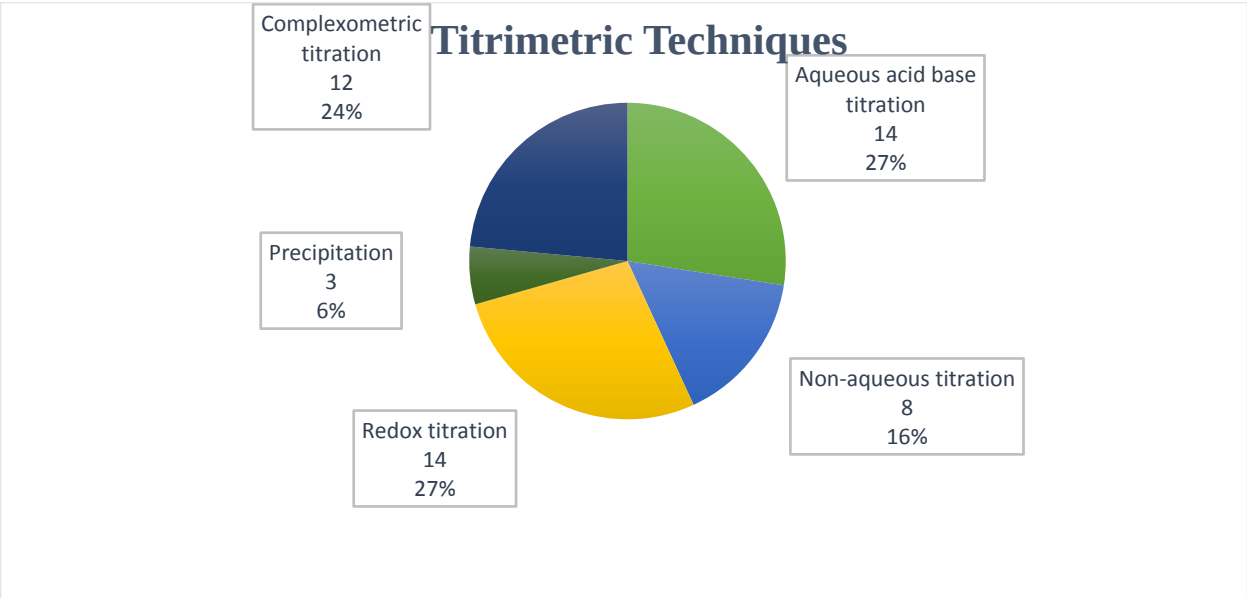


Figure 6: Pie Chart Showing Frequency of Titrimetric Techniques

There is no subtype dominant in titrimetric techniques for the formulations included in this study.

According to the database obtained, titrimetric techniques are the second most widely used technique after chromatography. Because these are robust, save time and provide precision. In the European Pharmacopoeia, about 70% of the drug products are assayed by these techniques. Around 40% of the organic compounds having low molecular weight are analyzed by aqueous or non-aqueous titration in accordance with USP (United State Pharmacopoeia) (Qarah & El-Maaiden, 2023). The database also indicated the wide use of redox and complexometric titration as they are precise methods and produce satisfactory results in analytical chemistry. Precipitation titration has the least use in comparison to other titrimetric methods.

3.5 Other Types

Immunological and gravimetric methods are the least used assay type among others. As gravimetric method is time consuming and only limited elements can be analyzed, its use has been limited as an assay method. Both immunological and gravimetric methods are replaced by other highly selective and informative methods in pharmacopoeias.

3.6 Discussion

According to S. Gorog/ Journal of Pharmaceutical and Biomedical Analysis 36 (2005) 931–937, analytical methods recommended in various proportions for performing assay of bulk drug materials In Ph Eur 4 and USP XXVII.

Table 1: Proportion of different analytical methods recommended for assay of bulk drug materials in Ph.Eur 4 and USP XXVII

Method	**Ph.Eur**	**USP**
HPLC	15.5%	44%
GC	2%	2.5%
Titration	69.5%	40.5%
Acid Base	57.5%	29.5%
Non-aqueous	36.5%	24%
Redox	6.5%	5.5%
Uv-vis Spectrophotometry	9.5%	8.5%
Microbiological assay	3%	2.5%
Other (IR, NMR, atomic absorption spectroscopy, gravimetry)	0.5%	2%

The above data indicated that, European pharmacopoeia (Ph.Eur 4) has titrimetric technique as the most used assay technique for bulk drug material whereas United State pharmacopoeia (USP XXVIII) has HPLC or chromatographic technique as the most prevalent one. The database obtained from our study indicated RP-HPLC as the most utilized technique.

HPLC is the second most used technique in Ph.Eur. In USP, titrimetric method is more frequent after chromatography which is same as our study data.

Spectrometry comes as the third most used technique and is less frequent than chromatographic and titrimetric methods. Our study data also showed the same.

Lastly, microbial assay, gravimetry and other techniques are used in a very less frequency and in specific sections. Our study also found similar results.

Chapter 4 Conclusion

The prepared database from this study does not give conclusive results after analysis of the frequency of assay types and sub types used in the quantitative measurement of drugs. The database only includes 209 formulations out of 1247 formulations in BP. Conclusive results would be obtained after including all the 1247 formulations present in BP. The completion of the database would be useful for the students and teachers in order to study and analyze the use of assay techniques on a case-by-case basis. It would provide knowledge on different types of assay techniques and their subsequent use in different types of formulations. The database would be also useful for method development analysis as considering the advantages and disadvantages of a certain method for a particular category of drug would provide better judgement for the selection of assay methods for that particular category. So, more convenient methods would be developed for existing drugs. Along with that, new methods can also be developed for new drugs by observing the assay types used for a particular class of drugs.

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Appendix

Prolonged-release Ibuprofen Capsules	capsule	chromatographic	reverse phase HPLC
Ibuprofen Cream	cream	chromatographic	reverse phase HPLC
Ibuprofen Gel	gel	chromatographic	reverse phase HPLC
Ibuprofen Oral suspension	suspension	chromatographic	reverse phase HPLC
Ibuprofen Tablets	tablet	chromatographic	reverse phase HPLC
prolonged-release Ibuprofen Tablets	tablet	chromatographic	reverse phase HPLC
Idoxuridine Eye drops	eye drops	chromatographic	reverse phase HPLC
Ifosfamide Injection	injection/infusion	chromatographic	reverse phase HPLC
Imipramine Tablets	tablet	spectroscopic	UV
Indapamide Tablets	tablet	chromatographic	reverse phase HPLC
Indometacin Capsules	capsule	spectroscopic	UV
Indometacin Suppositories	suppository	spectroscopic	UV
Indoramin Tablets	tablet	spectroscopic	UV

Inositol Nicotinate Tablets	tablet	titrimetric	non aqueous titration
Injectable Insulin Preparations	injection/infusion	chromatographic	reverse phase HPLC
Insulin Injection	injection/infusion	chromatographic	reverse phase HPLC
Insulin Aspart injection	injection/infusion	chromatographic	reverse phase HPLC
Biphasic Insulin Injection	injection/infusion	chromatographic	reverse phase HPLC
Biphasic Isophane Insulin Injection	injection/infusion	chromatographic	reverse phase HPLC
Isophane Insulin Injection	injection/infusion	chromatographic	reverse phase HPLC
Insulin lispro injection	injection/infusion	chromatographic	reverse phase HPLC
Protamine Zinc Insulin Injection	injection/infusion	chromatographic	reverse phase HPLC
Insulin Zinc Suspension	suspension	chromatographic	reverse phase HPLC
Insulin Zinc Suspension (Amorphous)	suspension	chromatographic	reverse phase HPLC
Insulin Zinc Suspension (Crystalline)	suspension	chromatographic	reverse phase HPLC
Interferon Alpha-2a Injection	injection/infusion	immunological	
Aqueous Idoine Oral Solution	solution	titrimetric	redox titration
Alcoholic Iodine Solution	solution	titrimetric	redox titration
Iodised Oil Fluid Injection	injection/infusion	titrimetric	redox titration
Iofendylate Injection	injection/infusion	titrimetric	redox titration
Iopamidol Injection	injection/infusion	titrimetric	precipitation
Iopamidol Oral Solution	solution	titrimetric	precipitation

Iopanoic Acid Tablets	tablet	titrimetric	redox titration
Ipratropium Nebuliser Solution	solution	chromatographic	reverse phase HPLC
Ipratropium Powder for Inhalation	powder	chromatographic	reverse phase HPLC
Ipratropium Pressurized Inhalation	miscellaneous	chromatographic	reverse phase HPLC
Iron Dextran Injection	injection/infusion	titrimetric	redox titration
Iron Dextran Injection	injection/infusion	spectroscopic	UV
Iron Sucrose Injection	injection/infusion	titrimetric	redox titration
Iron Sucrose Injection	injection/infusion	chromatographic	reverse phase HPLC
Isoconazole Pessaries	pessary	chromatographic	reverse phase HPLC
Isoniazid Injection	injection/infusion	titrimetric	redox titration
Isoniazid Oral Solution	solution	chromatographic	reverse phase HPLC
Isoniazid Tablets	tablet	titrimetric	redox titration
Isoprenaline Injection	injection/infusion	chromatographic	reverse phase HPLC
Isosorbide Dinitrate Injection	injection/infusion	chromatographic	reverse phase HPLC
Isosorbide Dinitrate Tablets	tablet	chromatographic	reverse phase HPLC
Isosorbide Dinitrate Sublingual Tablets	tablet	chromatographic	reverse phase HPLC
Isosorbide Mononitrate Tablets	tablet	chromatographic	reverse phase HPLC
Prolonged-realese Isosorbide Mononitrate Tablets	tablet	chromatographic	reverse phase HPLC
Isotretinoin Capsules	capsule	spectroscopic	UV

Isotretinoin Gel	gel	spectroscopic	UV
Isradipine Tablets	tablet	chromatographic	reverse phase HPLC
Kaolin Mixture	suspension	titrimetric	complexometric titration
Kaolin Mixture	suspension	titrimetric	aqueous acid base titration
Kaolin and Morphine Mixture	suspension	spectroscopic	UV
Kaolin and Morphine Mixture	suspension	titrimetric	aqueous acid base titration
Kaolin Poultice (Confusion)	miscellaneous	titrimetric	aqueous acid base titration
Ketamine Injection	injection/infusion	spectroscopic	UV
Ketoprofen Capsule	capsule	spectroscopic	UV
Ketoprofen Gel	gel	chromatographic	reverse phase HPLC
Labetolol Injection	injection/infusion	spectroscopic	UV
Lebetolol Tablets	tablet	spectroscopic	UV
Lecidipine Tablets	tablet	chromatographic	normal phase HPLC
Lactic acid Pessaries	pessary	titrimetric	aqueous acid base titration
Lactulose Oral Powder	powder	chromatographic	reverse phase HPLC
Lamivudine Tablets	tablet	chromatographic	reverse phase HPLC
Lamotrigine Tablets	tablet	chromatographic	reverse phase HPLC
Gastro-resistant Lansoprazole Capsule	capsule	chromatographic	reverse phase HPLC
Gastro-resistant Lansoprazole Tablets	tablet	chromatographic	reverse phase HPLC

Leuprorelin Injection	injection/infusion	chromatographic	reverse phase HPLC
Levobunolol Eye Drops	eye drops	chromatographic	reverse phase HPLC
Levodpa Capsules	capsule	titrimetric	non aqueous titration
Levodopa Tablets	tablet	titrimetric	non aqueous titration
Levomenthol Cream	cream	chromatographic	gas chromatography
Levomepromazine Injection	injection/infusion	spectroscopic	UV
Levomepromazine Tablets	tablet	spectroscopic	UV
Levonorgestrel Tablets	tablet	chromatographic	reverse phase HPLC
Levonorgestrel and Ethinylestradiol Tablets	tablet	chromatographic	reverse phase HPLC
Levothyroxine Tablets	tablet	chromatographic	reverse phase HPLC
Lidocaine Gel	gel	titrimetric	aqueous acid base titration
Lidocaine Injection	injection/infusion	titrimetric	non aqueous titration
Lidocaine Ointment	ointment	chromatographic	reverse phase HPLC
Sterile Lidocaine Solution	solution	titrimetric	non aqueous titration
Lidocaine and Adrenaline Injection/ Lidocaine and Epinephrine Injection	injection/infusion	titrimetric	non aqueous titration
Lidocaine and Adrenaline Injection/ Lidocaine and Epinephrine Injection	injection/infusion	chromatographic	reverse phase HPLC
Lidocaine and Chlorhexidine Gel	gel	chromatographic	reverse phase HPLC
Lidocaine and Chlorhexidine Gel	gel	chromatographic	reverse phase HPLC

Lincomycin Capsules	capsule	chromatographic	gas chromatography
Licomycin Injection	injection/infusion	chromatographic	gas chromatography
White Liniment	ointment	gravimetric	
Liothyronine Tablets	tablet	chromatographic	reverse phase HPLC
Lisinopril Oral Solution	solution	chromatographic	reverse phase HPLC
Lisinopril Tablets	tablet	chromatographic	reverse phase HPLC
Lithium Carbonate Tablets	tablet	titrimetric	aqueous acid base titration
Prolonged-release Lithium Carbonate Tablets	tablet	titrimetric	aqueous acid base titration
Lithium Citrate Oral Solution	solution	spectroscopic	atomic
Lofepramine Tablets	tablet	chromatographic	reverse phase HPLC
Lomustine Capsules	capsule	spectroscopic	UV
Loperamide Capsules	capsule	chromatographic	reverse phase HPLC
Loprazolam Tablets	tablet	spectroscopic	UV
Loratadine Tablets	tablet	chromatographic	reverse phase HPLC
Lorazepam Injection	injection/infusion	chromatographic	reverse phase HPLC
Lorazepam Tablets	tablet	spectroscopic	UV
Lormetazepam Tablets	tablet	chromatographic	reverse phase HPLC
Losartan Potassium Tablets	tablet	chromatographic	reverse phase HPLC
Lymecycline Capsules	capsule	chromatographic	reverse phase HPLC

Magaldrate Oral Suspension	suspension	titrimetric	aqueous acid base titration
Aromatic Magnesium Carbonate Mixture	suspension	titrimetric	aqueous acid base titration
Aromatic Magnesium Carbonate Mixture	suspension	titrimetric	complexometric titration
Magnesium Chloride Injection	injection/infusion	titrimetric	complexometric titration
Magnesium Glycerophosphate Oral Solution	solution	titrimetric	complexometric titration
Chewable Magnesium Glycerophosphate Tables	tablet	titrimetric	complexometric titration
Magnesium Hydroxide Mixture	suspension	titrimetric	aqueous acid base titration
Magnesium Sulphate Injection	injection/infusion	titrimetric	complexometric titration
Magnesium Sulphate Mixture	suspension	titrimetric	complexometric titration
Magnesium Sulphate Mixture	suspension	titrimetric	complexometric titration
Magnesium Sulphate Paste	paste	titrimetric	complexometric titration
Magnesium Sulphate Paste	paste	titrimetric	redox titration
Magnesium Tisilicate Mixture	suspension	titrimetric	aqueous acid base titration
Magnesium Tisilicate Mixture	suspension	titrimetric	complexometric titration
Compound Magnesium Trisilicate Oral Powder	powder	gravimetric	
Compound Magnesium Trisilicate Oral Powder	powder	titrimetric	aqueous acid base titration
Compound Magnesium Trisilicate Tablets	tablet	titrimetric	complexometric titration
Compound Magnesium Trisilicate Tablets	tablet	titrimetric	complexometric titration
Malathaion Lotion	lotion	chromatographic	reverse phase HPLC

Malathion Shampoo	miscellaneous	chromatographic	reverse phase HPLC
Mannitol Intravenous Infusion	injection/infusion	titrimetric	redox titration
Mebeverine Tablets	tablet	spectroscopic	UV
Medroxyprogesterone Injection	injection/infusion	chromatographic	reverse phase HPLC
Medroxyprogesterone Tablets	tablet	chromatographic	reverse phase HPLC
Mefenamic Acid Capsules	capsule	titrimetric	aqueous acid base titration
Mefenamic Acid Tablets	tablet	titrimetric	aqueous acid base titration
Megestrol Tablets	tablet	chromatographic	reverse phase HPLC
Meglumine Amidotrizoate Injection	injection/infusion	titrimetric	redox titration
Meglumine Iodipamide Injection	injection/infusion	titrimetric	redox titration
Melatonin Capsules	capsule	chromatographic	reverse phase HPLC
Meloxicam Tablets	tablet	chromatographic	reverse phase HPLC
Melphalan Injection	injection/infusion	chromatographic	reverse phase HPLC
Melphalan Tablets	tablet	chromatographic	reverse phase HPLC
Menadiol Phosphate Injection	injection/infusion	spectroscopic	UV
Menadiol Phosphate Tablets	tablet	spectroscopic	UV
Menotrophin Injection	injection/infusion	immunological	
Meptazinol Injection	injection/infusion	spectroscopic	UV
Meptazinol Tablets	tablet	spectroscopic	UV

Mepyramine Tablets	tablet	spectroscopic	UV
Mercaptopurine Oral Suspension	suspension	chromatographic	reverse phase HPLC
Mercaptopurine Tablets	tablet	chromatographic	reverse phase HPLC
Mesalazine Enema	enema	chromatographic	reverse phase HPLC
Mesalazine Foam Enema	enema	chromatographic	reverse phase HPLC
Prolonged-release Mesalazine Granules	powder	chromatographic	reverse phase HPLC
Mesalazine Suppositories	suppository	chromatographic	reverse phase HPLC
Gastro-resistant Mesalazine Tablets	tablet	chromatographic	reverse phase HPLC
Prolonged-release Mesalazine Tablets	tablet	chromatographic	reverse phase HPLC
Metaraminol Injection	injection/infusion	spectroscopic	UV
Metformin Oral Solution	solution	chromatographic	ion exchange
Metformin Tablets	tablet	spectroscopic	UV
Methadone Injection	injection/infusion	spectroscopic	UV
Methadone Linctus	spirit/elixir/linctus	spectroscopic	UV
Methadone Oral Solution (1 mg per ml)	solution	chromatographic	reverse phase HPLC
Methadone Tablets	tablet	spectroscopic	UV
Methotrexate Injection	injection/infusion	chromatographic	reverse phase HPLC
Methotrexate Tablets	tablet	chromatographic	reverse phase HPLC
Methoxamine Injection	injection/infusion	spectroscopic	UV

Methyl Salicylate Liniment	ointment	chromatographic	gas chromatography
Methyl Salicylate Ointment	ointment	chromatographic	gas chromatography
Methyldopa Tablets	tablet	spectroscopic	UV
Methyldopate Injection	injection/infusion	chromatographic	reverse phase HPLC
Methylpheobarbital Tablets	tablet	chromatographic	reverse phase HPLC
Methylprednisolone Tablets	tablet	spectroscopic	UV
Methylprednisolone Acetate Injection	injection/infusion	chromatographic	reverse phase HPLC
Methylthioninium Injection	injection/infusion	titrimetric	redox titration
Methysergide Tablets	tablet	spectroscopic	UV
Metipranolol Eye Drops	eye drops	chromatographic	reverse phase HPLC
Metoclopramide Injection	injection/infusion	chromatographic	reverse phase HPLC
Metoclopramide Oral Solution	solution	spectroscopic	UV
Metoclopramide Tablets	tablet	chromatographic	reverse phase HPLC
Metoprolol Injection	injection/infusion	spectroscopic	UV
Metoprolol Tartrate Tablets	tablet	spectroscopic	UV
Prolonged-release Metoprolol Tartrate Tablets	tablet	spectroscopic	UV
Metronidazole Gel	gel	chromatographic	reverse phase HPLC
Metronidazole Intravenous Infusion	injection/infusion	spectroscopic	UV
Metronidazole Oral Suspension	suspension	chromatographic	reverse phase HPLC

Metronidazole Suppositories	suppository	titrimetric	non aqueous titration
Metronidazole Tablets	tablet	titrimetric	non aqueous titration
Metyrapone Capsules	capsule	spectroscopic	UV
Mexenone Cream	cream	spectroscopic	UV
Mexiletine Capsules	capsule	spectroscopic	UV
Mexiletine Injection	injection/infusion	spectroscopic	UV
Mianserin Tablets	tablet	chromatographic	gas chromatography
Miconazole Cream	cream	chromatographic	reverse phase HPLC
Miconazole Oromucosal Gel	gel	chromatographic	reverse phase HPLC
Miconazole and Hydrocortisone Cream	cream	chromatographic	reverse phase HPLC
Miconazole and Hydrocortisone Ointment	ointment	chromatographic	reverse phase HPLC
Miconazole and Hydrocortisone Acetate Cream	cream	chromatographic	reverse phase HPLC
Midazolam Injection	injection/infusion	chromatographic	reverse phase HPLC
Midazolam Oral Solution	solution	chromatographic	reverse phase HPLC
Prolonged-release Minnocycline Capsules	capsule	chromatographic	reverse phase HPLC
Minocycline Tablets	tablet	chromatographic	reverse phase HPLC
Minoxidil Scalp Application	miscellaneous	chromatographic	reverse phase HPLC
Mirtazapine Tablets	tablet	chromatographic	reverse phase HPLC
Orodispersible Mirtazapine Tablets	tablet	chromatographic	reverse phase HPLC

Mitobronitol Tablets	tablet	titrimetric	precipitation
Mitoxantrone Infusion	injection/infusion	chromatographic	reverse phase HPLC
Mometason Scalp Application	ointment	chromatographic	reverse phase HPLC
Mometason Cream	cream	chromatographic	reverse phase HPLC
Mometason Aqueous Nasal Spray	spray	chromatographic	reverse phase HPLC
Mometason Ointment	ointment	chromatographic	reverse phase HPLC
Morphine Suppositories	suppository	chromatographic	reverse phase HPLC