A REVIEW ON DRUG FORMULATION AND ASSAY TYPE ACCORDING TO BRITISH PHARMACOPOEIA

By

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A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (Hons)

School of Pharmacy
BRAC University
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Declaration

It is hereby declared that

1. The thesis submitted is my/our own original work while completing 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.

Student's Full Name & Signature:

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Approval

The thesis titled “A REVIEW ON DRUG FORMULATION AND ASSAY TYPE ACCORDING TO BRITISH PHARMACOPOEIA” submitted by Tanjila Jaman (19146021) of Spring, 2023 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy on September,23.

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Ethics Statement

This study did not involve any human participants, human specimens or tissue, vertebrate animals or cephalopods, vertebrate embryos or tissues and field research.

Abstract

The goal of this study was to create a database of 119 formulations by classifying each formulation's assay types and sub types from the 1247 specific formulation monographs found in the British Pharmacopoeia. According to this database, chromatographic procedures are most frequently recommended. The most suggested techniques for analyzing drugs after chromatography are titrimetric and spectroscopic techniques. Creation of this database that will be helpful to students and those who develop analytical methods. This project aimed to advance education.

Keywords: BP, assay type, database.

Dedication

Dedicated to my father whose hard work and ambitious thought regarding his child helped to reach me where I am standing today and my mother whose sacrifices gave me a strong base to create my stage in society.

Acknowledgement

I am grateful to almighty Allah for providing me the opportunity to work with such wonderful people from the school of pharmacy who have always been idealistic and encouraging throughout my journey.

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List of Acronyms

BP	British Pharmacopoeia
MHRA	Medicines and Healthcare Products Regulatory Agency
TLC	Thin-layer chromatography
HPLC	High-pressure liquid chromatography
RP-HPLC	Reversed-phase chromatography
AES	Atomic Emission Spectroscopy
AAS	Atomic Absorption Spectroscopy
ICP-OES	Inductively Coupled Plasma-Optical Emission Spectroscopy
AFS	Atomic Fluorescence Spectroscopy
ICP-MS	Inductively Coupled Plasma-Mass Spectrometry

Chapter 1

Introduction

1.1 Background

The British Pharmacopoeia (BP) is a comprehensive set of quality standards for medications and pharmaceuticals used in the UK. The British Pharmacopoeia Commission, a Medicines and Healthcare Products Regulatory Agency (MHRA) division, is responsible for its publication. The key objectives of the BP are to advance public health and secure the dependability and safety of UK medicines. It specifies standards for materials used to manufacture medicines, including identity, purity, potency, and quality assurance. The BP is constantly updated to reflect advancements in research and modifications to medical practices. It is accessible to many consumers because it is also available electronically. (Ho, 1961)

1.2 Assay

In a laboratory context, an assay is a method of investigation used to determine whether a target element is present, how much there is, or how it functions. It is employed in pharmacy, mining, medicine, and numerous branches of biology. The term can refer to either the analyte or the measurand. The assay aims to express the intensity of the target as a meaningful measurement. For optimal procurement, effective stock management, and sensible medicine use, accurate quantification of pharmaceutical demand is crucial. (Riley et al., 2014)
Different assays are present for example chromatographic, spectrometric, gravimetric, biological, titrimetric, and polarimetric measurements.

1.3 Chromatography

Chromatography is one of the easiest assay identification process. According to the basic concept of chromatography, molecules in a mixture applied to a surface or a solid, and a fluid stationary phase (stable phase), separate from one another while moving with the assistance of a mobile phase. Chromatography is an essential scientific method that allows for the purification, separation, and identification of a mixture's constituent parts for qualitative and quantitative test. The molecular features related to adsorption (liquid-solid), partition (liquid-solid), and affinity or differences among their molecular weights are the factors that have an impact on this separation process. There are three main components to form chromatography technique. These are stationary phase, mobile phase, separated molecules. Stationary phase is the phase which does not move with the components. It is a fixed solid phase. Where as mobile phase moves with components and this phase is made up of liquid or gaseous components. Chromatography is very effective assay type for the small molecules as example amino acid, fatty acid and carbohydrates. The primary objective of employing chromatography as a

quantitative analytical technique, in addition to its separation capabilities, is to attain a reasonable level of separation within a suitable timeframe. Several chromatographic methods have been developed for this purpose. Several chromatographic techniques can be employed for separation and analysis purposes. These techniques encompass column chromatography, thin-layer chromatography (TLC), paper chromatography, gas chromatography, ion exchange chromatography, gel permeation chromatography, high-pressure liquid chromatography, and affinity chromatography.

1.3.1 Column Chromatography

Column chromatography consists of a stationary solid phase that adsorbs and separates the compounds passing through it with the help of a liquid mobile phase. On the basis of their chemical nature, compounds get adsorbed and elution is based on differential adsorption of a substance by the adsorbent. Proteins include several distinctive attributes: size, shape, net charge, stationary phase employed, and binding capability. Consequently, each of these characteristic constituents can be subjected to purification by chromatographic techniques. Column chromatography is the procedure most commonly utilized among these several techniques. This particular methodology is employed for the process of purifying biomolecules.

1.3.2 Ion-exchange chromatography

The principle of ion-exchange chromatography is based on the interaction of intended protein's charge and matrix that is solid support material. Matrix and protein possess opposite charge which is responsible for separation and this ionic interaction among them established the protein's combination for the column. Proteins can be effectively isolated from the column through the manipulation of various factors such as pH, ion salt concentration, or the ionic

strength of the buffer solution. Matrices that possess a positive charge and facilitate ion exchange are referred to as anion-exchange matrices, as they effectively adsorb proteins with a negative charge. On the contrary, positively charged protein’s are bound to the negatively charged matrices called cation-exchange matrices.

1.3.3 Gas chromatography

Gas chromatography is a form of chromatography that operates on the principle of gas-liquid partitioning. The carrier phase of the system comprises gases for example helium or nitrogen. At high pressure, the inert gas mobile phase is introduced into a column. The specimen under examination is subjected to vaporization, resulting in its transition into a mobile phase in the form of a gas. The constituents present in the specimen are distributed throughout the mobile phase and the stationary phase is immobilized on the solid support. Gas chromatography is a versatile and efficient analytical technique that offers exceptional sensitivity and quick separation of small compounds. This technique is employed for the isolation of minute quantities of analytes.

1.3.4 Paper chromatography

Paper chromatography is a common analytical method in chemical research. It involves the separation of mixtures into their individual components. In paper chromatography, a layer of cellulose that has been soaked with water serves as the support material. This approach utilized a dense filter paper as the supporting material, with water droplets occupying the paper's pores to form the stationary "liquid phase." The mobile phase is comprised of a suitable fluid that is placed within a developing tank. Paper chromatography is a type of chromatography that falls under the category of "liquid-liquid" chromatography.

1.3.5 High-pressure liquid chromatography (HPLC)

This chromatography approach allows for the structural and functional study and the purification of numerous molecules in a short period. This approach perfectly separates and perfectly identifies amino acids, lipids, nucleic acids, carbohydrates, steroids, proteins and other physiologically active substances. HPLC utilizes a high pressure (10-400 atmospheres) and a fast flow rate (0.1-5.0 cm/sec) for the mobile phase as it moves through the columns. This technology improves the separation capability of high-performance liquid chromatography (HPLC) by using microscopic particles and by applying high pressure to the rate of solvent flow. Two different forms of HPLC exist; one is normal phase HPLC. When using an organic solvent as eluent in normal phase HPLC with a silica or amino-group bonded phase column, the first components to leave the column are the saturated hydrocarbons [Herod et al., 1988]. Another one is reverse phase HPLC. The most common HPLC separation technique is reversed-phase chromatography (RP-HPLC), which separates a wide range of chemicals. Compounds suitable for RP-HPLC separation should have some (accessible) hydrophobic moieties, but the presence of polar groups does not rule out RP-HPLC use. RP-HPLC can analyze compounds with significantly varying polarity. (Coskun, 2016)

1.4 Spectroscopic

Spectroscopy is the scientific discipline that investigates the interaction between matter and electromagnetic radiation, which has evolved from the phenomenon of visible light scattering. The utilization of many analytical techniques is a common practice in the field, including UV-Vis spectroscopy, infrared spectroscopy, nuclear magnetic resonance spectroscopy, atomic absorption spectroscopy, flame emission spectroscopy, mass spectrometry, fluorescence spectroscopy, and electron microscopy. The present investigation reveals two essential techniques, namely UV and atomic absorption spectroscopy, as demonstrated by the obtained

results. Atomic and UV spectroscopy are crucial analytical techniques for identifying pharmaceuticals employed in assays, as they provide significant insights into the tested material's composition and quantity. UV spectroscopy encompasses the absorption of ultraviolet or visible light by molecules within a sample, which is a technique applicable to qualitative and quantitative analysis. The operational mechanism involves the computation of the sample's absorption at many wavelengths of light, identification of electronic transitions, and acquisition of the absorption spectrum. The spectrum exhibits discernible peaks aligning with specific functional groups or chromophores in the medication molecule. The identification and assessment of drug purity can be accomplished by utilizing UV absorption, where in the drug's absorption characteristics are compared to reference spectra of established medicines or drug standards. In addition, the utilization of calibration curves derived from standard solutions enables the application of UV spectroscopy for quantitative analysis, facilitating the determination of the quantity of a pharmaceutical compound inside a given sample. Atomic spectroscopy is widely utilized analytical technique utilized for the purpose of investigating the elemental composition of a given sample, encompassing many types of substances, including those of medicinal nature. The techniques encompassed within this category include , Atomic Emission Spectroscopy (AES), Atomic Absorption Spectroscopy (AAS)Inductively Coupled Plasma-Optical Emission Spectroscopy (ICP-OES), Atomic Fluorescence Spectroscopy (AFS) and Inductively Coupled Plasma-Mass Spectrometry (ICP-MS). Spectroscopy of the light emitted from excited atoms is known as atomic emission spectroscopy (AES). Whereas, Atomic Absorption Spectroscopy (AAS) is a method used to detect light absorption by atoms in their ground state. The atomic fluorescence spectroscopy (AFS) approach is considered more sensitive for analyzing trace elements. Both methods can be employed to examine several elements and exhibit high sensitivity. Atomic spectroscopy is a commonly employed technique in drug assay identification to quantify the concentration of

trace elements, particularly heavy metals. These heavy metals in pharmaceutical products above permissible thresholds can pose significant risks to human health. (Izrio Filho et al., 2012; Lewen, 2011)

1.5 Titration

In the process of titration, an aqueous solution of unknown concentration is subjected to a chemical reaction with a solution of known concentration, with the primary objective of elucidating pertinent information about the unknown solution that usually relates to its concentration. Acid-base and redox titrations are well-recognized as two of the most prevalent types of titrations. In the context of acid-base titration, it is observed that one of the solutions involved in the process is characterized as an acid, while the other solution is classified as a base. A substance is introduced into a flask. The second solution is introduced into a burette and thereafter added dropwise into the flask until the titration reaction reaches its endpoint. It is imperative to select an appropriate indicator that effectively signifies the attainment of the equivalence point, wherein all the solution present in the flask has completely reacted with the solution being added dropwise. In an ideal titration, the point at which the indicator changes color (endpoint) and the point at which the stoichiometrically equivalent amounts of reactants have reacted (equivalence point) will coincide. In the event that an indicator is not selected appropriately, there will be a discrepancy between the end and equivalence points, resulting in the titration yielding imprecise data regarding the solution under investigation. In the context of redox titration, it is seen that one of the solutions functions as a reducing agent, while the other solution acts as an oxidizing agent. The point of equivalency is attained once an adequate number of oxidizing agents has been introduced to react with all of the reducing agents present. A redox indicator, capable of undergoing a color change as it transitions between its reduced and oxidized states, can be employed to identify the endpoint. Titrimetric methodologies

employed in drug testing encompass acid-base titration, oxidation-reduction (redox) titration, and complexometric titration. The selection of the appropriate option is contingent upon the specific attributes of the drug as well as the target analyte. The process of acid-base titration entails the reaction between a medical substance and a titrant of established concentration, with the purpose of determining the concentration of acid or base present in the given sample. A pH indicator is used to determine the endpoint. Redox titration is a chemical analysis technique that entails the transfer of electrons between a pharmaceutical compound and a titrant, such as iodine, which is commonly employed for the determination of vitamin C levels. The excess iodine is oxidized to ascorbic acid after being titrated with sodium thiosulfate until the iodine color disappears. Complexometric titration typically involves the creation of a stable complex between the drug component and titrant, which is commonly employed for the detection of metal ions or chelating agents. Ethylenediaminetetraacetic acid (EDTA) is commonly employed as a complexing agent in the field of pharmaceutical analysis. In order to ensure the precision and reliability of the results, titrimetric assays must exercise meticulous selection of titrants, markers, and experimental setups. The concentration of the drug component can be ascertained by using calibration curves or standard solutions, given the established stoichiometry of the reaction. (Caffrey & Borrelli, 2020)

1.6 Polarimetry

Enzymes catalyzing a wide variety of processes, such as peptidases, phosphohexose isomerase, glutamate decarboxylase, and glutamate alanine transaminase, have all been tested using a polarimetric assay. (Blass & Adams, 1976)

1.7 Aim and objectives

The purpose of this project is to create a database that will make it easy for scientists and students to identify the assay type of pharmaceutical compounds. The table includes information about each type of assay, and subtype, so that students can benefit from using it. They can discover the sort of assay for formulation and compile further information from the BP. Teachers can gather information in a short time as it has its own organized form. This database is prepared for having a organized form of drugs formulation, assay and sub assay type. This database will help to find out these information in a short time which would be helpful for scientists, teachers and students.

Chapter-2

Methodology

The following method was used for this study-

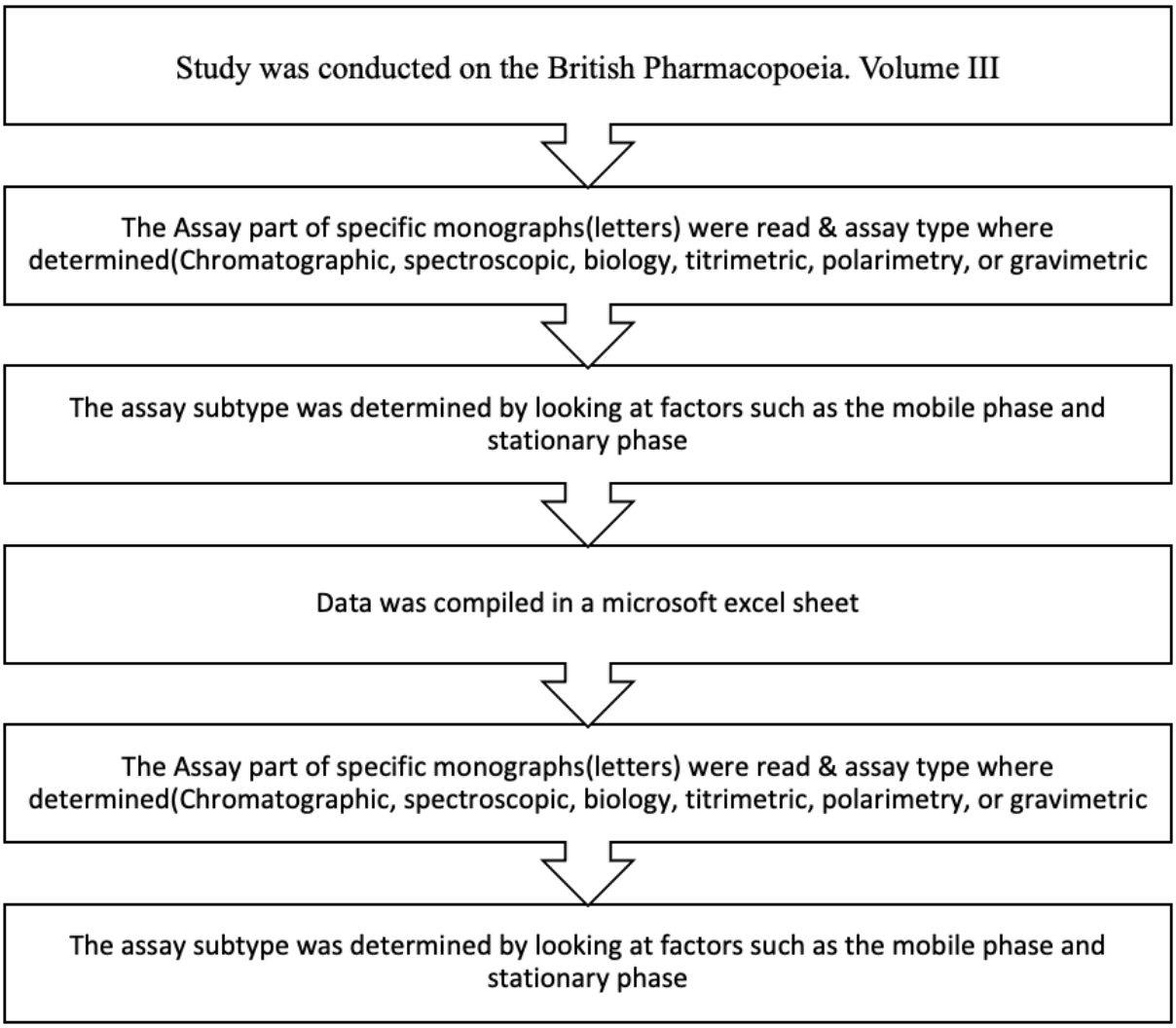

FIGURE 1.0 : Methodology

Chapter 3

Result and Discussion

This study was prepared by the help of BP which is shown below in the format of table.

The following database was created in this study**.**

Drug	**Dosage form**	**Assay type**	**Assay subtype**
Benzyl benzoate application	lotion	chromatographic	reverse phase HPLC
Benzylpenicillin injection	injection/infusion	chromatographic	reverse phase HPLC
Betahistine dihydrochloride tablets	tablet	chromatographic	reverse phase HPLC
Betamethasone eye drop	eye drops	chromatographic	reverse phase HPLC
Betamethasone injections	injection/infusion	chromatographic	reverse phase HPLC
Betamethasone tablet	tablet	chromatographic	reverse phase HPLC
Betamethasone and clioquinol cream	cream	chromatographic	reverse phase HPLC
Betamethasone and clioquinol cream	cream	chromatographic	reverse phase HPLC
Betamethasone and clioquinol ointment	ointment	chromatographic	reverse phase HPLC
Betamethasone and clioquinol ointment	ointment	chromatographic	reverse phase HPLC
Betamethasone sodium phosphate tablets	tablet	chromatographic	reverse phase HPLC
Betamethasone valerate scalp application	lotion	chromatographic	reverse phase HPLC
Betamethasone valerate cream	cream	chromatographic	reverse phase HPLC
Betamethasone valerate lotion	lotion	chromatographic	reverse phase HPLC
Betamethasone valerate ointment	ointment	chromatographic	reverse phase HPLC
Betaxolol eye drops, solution	solution	chromatographic	reverse phase HPLC
Betaxolol eye drops, suspension	suspension	chromatographic	reverse phase HPLC
Bezafibrate tablet	tablet	spectroscopic	UV
Prolonged-release Bezafibrate tablet	tablet	spectroscopic	UV

Bisacodyl suppositories	suppository	titrimetric	non aqueous titration
Gastro-resistant Bisacodyl Tablets	tablet	chromatographic	reverse phase HPLC
Bleomycin Injection	injection/infusion	biological	
Bretylium Injection	injection/infusion	chromatographic	reverse phase HPLC
Bromocriptine Capsules	capsule	chromatographic	reverse phase HPLC
Bromocriptine Tablets	tablet	chromatographic	reverse phase HPLC
Brompheniramine Tablets	tablet	spectroscopic	UV
Budesonide Aqueous Nasal Spray	spray	chromatographic	reverse phase HPLC
Budesonide Nebuliser Suspension	suspension	chromatographic	reverse phase HPLC
Budesonide Powder for Inhalation	powder	chromatographic	reverse phase HPLC
Budesonide Pressurised Inhalation	suspension	chromatographic	reverse phase HPLC
Buffered Cream	cream	assay not mentioned	not mentioned
Bumetanide Injection	injection/infusion	chromatographic	reverse phase HPLC
Bumetanide Oral Solution	solution	chromatographic	reverse phase HPLC
Bumetanide Tablets	tablet	chromatographic	reverse phase HPLC
Bumetanide	tablet	chromatographic	reverse phase HPLC
Bumetanide and Prolonged-release Potassium	tablet	spectroscopic	atomic
Bupivacaine Injection	injection/infusion	chromatographic	reverse phase HPLC
Bupivacaine Heavy Injection	injection/infusion	chromatographic	reverse phase HPLC
Bupivacaine Heavy Injection	injection/infusion	polarimetry	optical rotation
Bupivacaine and Adrenaline Injection	injection/infusion	chromatographic	reverse phase HPLC
Bupivacaine and Epinephrine Injection	injection/infusion	chromatographic	reverse phase HPLC
Buprenorphine and diamorphine Injection	injection/infusion	chromatographic	reverse phase HPLC
Bupivacaine and Fentanyl Injection	injection/infusion	spectroscopic	UV
Bupivacaine and Fentanyl Injection	injection/infusion	chromatographic	reverse phase HPLC
Buprenorphine Injection	injection/infusion	chromatographic	reverse phase HPLC

Buprenorphine transdermal patches	implant/patch	chromatographic	reverse phase HPLC
Buprenorphine Sublingual Tablets	tablet	chromatographic	reverse phase HPLC
Busulfan Tablets	tablet	chromatographic	gas chromatography
Caffeine Citrate Injection	injection/infusion	chromatographic	reverse phase HPLC
Caffeine Citrate Oral Solution	solution	chromatographic	reverse phase HPLC
Aqueous Calamine Cream	cream	gravimetric	
Calamine Lotion	lotion	gravimetric	
Calamine Ointment	ointment	gravimetric	
Calamine and Coal Tar Ointment	ointment	gravimetric	
Calcitonin (Salmon) Injection	injection/infusion	chromatographic	reverse phase HPLC
Calcitriol Capsules.	capsule	chromatographic	normal phase HPLC
Calcium and Colecalciferol Tablets	tablet	titrimetric	complexometric titration
Calcium and Colecalciferol Tablets	tablet	chromatographic	reverse phase HPLC
Calcium and Ergocalciferol Tablets	tablet	titrimetric	complexometric titration
Calcium and Ergocalciferol Tablets	tablet	chromatographic	reverse phase HPLC
Chewable Calcium Carbonate Tablets	tablet	titrimetric	complexometric titration
Calcium Carbonate	tablet	spectroscopic	atomic
Calcium Carbonate and Calcium Chloride	tablet	spectroscopic	atomic
Calcium Chloride Injection	injection/infusion	titrimetric	complexometric titration
Calcium Folinate Injection	injection/infusion	chromatographic	reverse phase HPLC
Calcium Folinate Tablets	tablet	chromatographic	reverse phase HPLC
Calcium Gluconate Injection	injection/infusion	titrimetric	complexometric titration
Calcium Gluconate Tablets	tablet	titrimetric	aqueous acid base titration
Calcium Gluconate Tablets Effervescent	effervescent tablet	titrimetric	complexometric titration
Calcium Hydroxide Solution	solution	titrimetric	aqueous acid base titration
Calcium Lactate Tablets	tablet	titrimetric	complexometric titration

Concentrated Camphor Water	solution	assay not mentioned	not mentioned
Captopril Oral Solution	solution	chromatographic	reverse phase HPLC
Captopril Tablets	tablet	chromatographic	reverse phase HPLC
Carbamazepine Tablets	tablet	chromatographic	reverse phase HPLC
Carbaryl Lotion	lotion	chromatographic	reverse phase HPLC
Carbimazole Tablets	tablet	chromatographic	reverse phase HPLC
Carbomer Eye Drops	eye drops	Assay not mentioned	not mentioned
Carboplatin Injection	injection/infusion	chromatographic	reverse phase HPLC
Carmellose Sodium Eye Drops	eye drops	spectroscopic	UV
Carteolol Eye Drops	eye drops	chromatographic	reverse phase HPLC
Cefaclor Capsules	capsule	chromatographic	reverse phase HPLC
Cefaclor Oral Suspension	suspension	chromatographic	reverse phase HPLC
Prolonged-release Cefaclor Tablets	tablet	chromatographic	reverse phase HPLC
Cefadroxil Capsules	capsule	chromatographic	reverse phase HPLC
Cefadroxil Oral Suspension	capsule	chromatographic	reverse phase HPLC
Cefalexin Capsules	capsule	chromatographic	reverse phase HPLC
Cefalexin Oral Suspension	suspension	chromatographic	reverse phase HPLC
Cefalexin Tablets	tablet	chromatographic	reverse phase HPLC
Cefazolin Injection	injection/infusion	chromatographic	reverse phase HPLC
Cefotaxime Injection	injection/infusion	chromatographic	reverse phase HPLC
Cefoxitin Injection	injection/infusion	chromatographic	reverse phase HPLC
Cefradine Capsules	injection/infusion	chromatographic	reverse phase HPLC
Cefradine Injection	injection/infusion	chromatographic	reverse phase HPLC
Cefradine Oral Suspension	suspension	chromatographic	reverse phase HPLC
Ceftazidime Injection	injection/infusion	chromatographic	reverse phase HPLC

Ceftazidime Injection	injection/infusion	spectroscopic	atomic
Ceftriaxone Injection	injection/infusion	chromatographic	reverse phase HPLC
Cefuroxime Eye Drops	eye drops	chromatographic	reverse phase HPLC
Cefuroxime Injection	injection/infusion	chromatographic	reverse phase HPLC
Cefuroxime Intracameral Injection	injection/infusion	chromatographic	reverse phase HPLC
Cefuroxime Axetil Oral Suspension	suspension	chromatographic	reverse phase HPLC
Cefuroxime Axetil Tablets	tablet	chromatographic	reverse phase HPLC
Celiprolol Tablets	tablet	chromatographic	reverse phase HPLC
Cetirizine Oral Solution	solution	chromatographic	reverse phase HPLC
Cetirizine Tablets	tablet	chromatographic	reverse phase HPLC
Cetomacrogol Emulsifying Ointment	ointment	assay not mentioned	not mentioned
Cetomacrogol Emulsifying Wax	cream	assay not mentioned	not mentioned
Cetrimide Cream	cream	titrimetric	aqueous acid base titration
Cetrimide Emulsifying Ointment	ointment	titrimetric	aqueous acid base titration
Cetrimide Solution	solution	titrimetric	aqueous acid base titration
Buprenorphine sublingual tablets	tablet	chromatographic	reverse phase HPLC
Caffeine Citrate Oral Solution	solution	chromatographic	reverse phase HPLC
Calcium chloride injections	injection/infusion	titrimetric	non aqueous titration
Cefradin oral suspension	suspension	chromatographic	reverse phase HPLC
Ceftazidime injection	injection/infusion	titrimetric	redox titration
Cefuroxime Axetil oral suspension	suspension	chromatographic	reverse phase HPLC
Cetrimide cream	cream	titrimetric	aqueous acid base titration
Cetrimide solution	solution	titrimetric	aqueous acid base titration

Table 1.0 : Database

3.1 Findings the percentage of assay type from taken drugs

The information is gathered from the British Pharmacopoeia in this project. In accordance with the assay types used, such as chromatographic, spectrometric, gravimetric, biological, titrimetric, and polarimetric measurements, I analyze the results. Chromatographic assays account for 68.9% of all assays, followed by spectroscopic (7.6%), titrimetric (14.3%), biological (0.8%), polarimetric (0.8%), gravimetric (3.4%) and assay not mentioned 4.2%

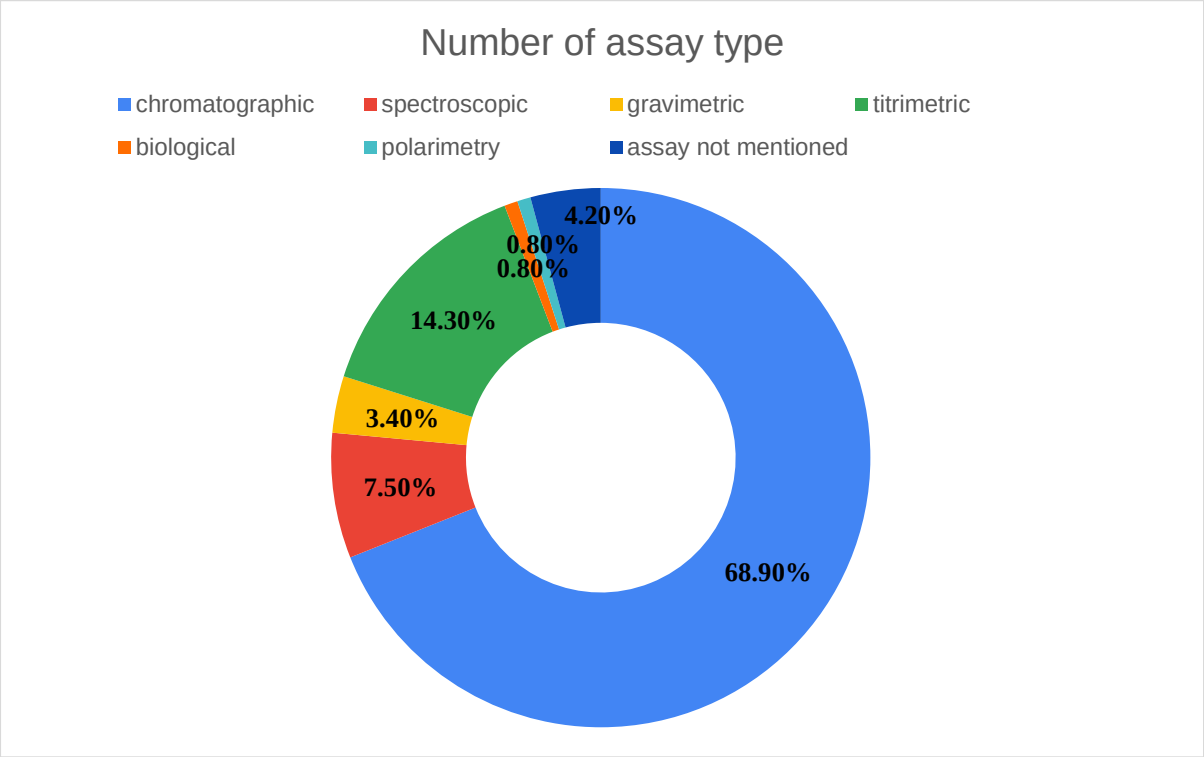

Figure 1.1: Number of assay types

Total number of assay studied was 119. The results show that chromatography is most frequently recommended because of its benefits.

The remarkable separation properties of chromatography enable the isolation and analysis of complicated mixtures. Drugs are typically mixed with other compounds in biological samples, yet chromatography is able to precisely separate and differentiate between various medication constituents. Since chromatographic methods are so sensitive, it is feasible to identify and measure chemicals even at very low quantities. This is crucial for pharmaceutical analysis since precise measurements are required to evaluate the potency and purity. Chromatography facilitates selectivity by allowing for the differentiation and separation of molecules according to their chemical properties. By combining a number of stationary and mobile phases, chromatography may successfully separate medications from influencing chemicals, enabling precise identification and quantification. Numerous techniques are used in chromatography, such as HPLC, GC, and TLC, which may be tailored to different drug compounds and are helpful for a range of drug tests. After analysis, chromatography leaves the material unspoiled, making it an ecologically beneficial analytical technique. This is especially beneficial when more testing or assurance is required or when there are limited samples available. It is a useful technique for detecting drugs in testing, although it is typically combined with other analytical methods like spectroscopy or mass spectrometry to improve precision and reliability. The precise requirements of the investigation and the characteristics of the substance under investigation define the methodology chosen (Coskun, O. 2016)

From the collected data we can see that after chromatographic technique the most recommended analysis method is titrimetric. This is due to advantages of this techniques such as -

Analysis can happen quickly, immediate conclusion of responses. Greater precision because decanting, filtering, precipitation, or similar activities cause less material loss. There is no need for labor-intensive open-flame heating or hot-air oven drying. Monitoring of endpoints in real-time using electrometric techniques or indicators. (Young, L. B. ,2021, April 7).

The third most recommended spectroscopy, which monitors and examines how electromagnetic radiation interacts with materials, is another method for spotting drug tests. Examples include Mass Spectrometry, NMR Spectroscopy, Infrared Spectroscopy, UV-Visible Spectroscopy, and Fluorescence Spectroscopy. It gives important details about the identity, purity, concentration, and structural features of drug molecules. Another method for figuring out the concentration or purity of a pharmaceutical substance is titrimetric analysis. A quantitative reaction occurs between the drug molecule and a titrant, a reagent with a known concentration.

Whereas less used techniques are polarimetry, biological methods and gravimetry. Gravimetry has some drawbacks,

It is unreliable for measuring medications at low concentrations. The method is less sensitive than other analytical techniques, making it challenging to detect and evaluate drug traces. In addition to being time-consuming and requiring complex sample preparation procedures, gravimetric techniques can also be exhausting, which makes them less practical for routine analysis. Mistakes can also be made throughout the method due to sample contamination, partial precipitation, and moisture content, among other factors (P. Vaníček, R. Kingdon, 2015)

.

As a result of these drawbacks, these approaches to drug analysis are not favored over analytical procedures that are more precise and efficient.

3.2 Findings the percentage of sub-assay type from taken drugs

Apart from these, there were sub types present in these techniques are aqueous acid base titration, non-aqueous titration, redox titration, complexometric titration, UV, fluorescence, normal phase HPLC, reverse phase HPLC, ion exchange, TLC, size exclusion, precipitation, atomic, ELISA, RIA, gas chromatography and optical rotation.

As the graph presented below shows, reverse phase HPLC is the technique that is most frequently utilized when it comes to assay subtypes. According to my research, over 80 medicines were discovered in 119 medications that were processed using this method.

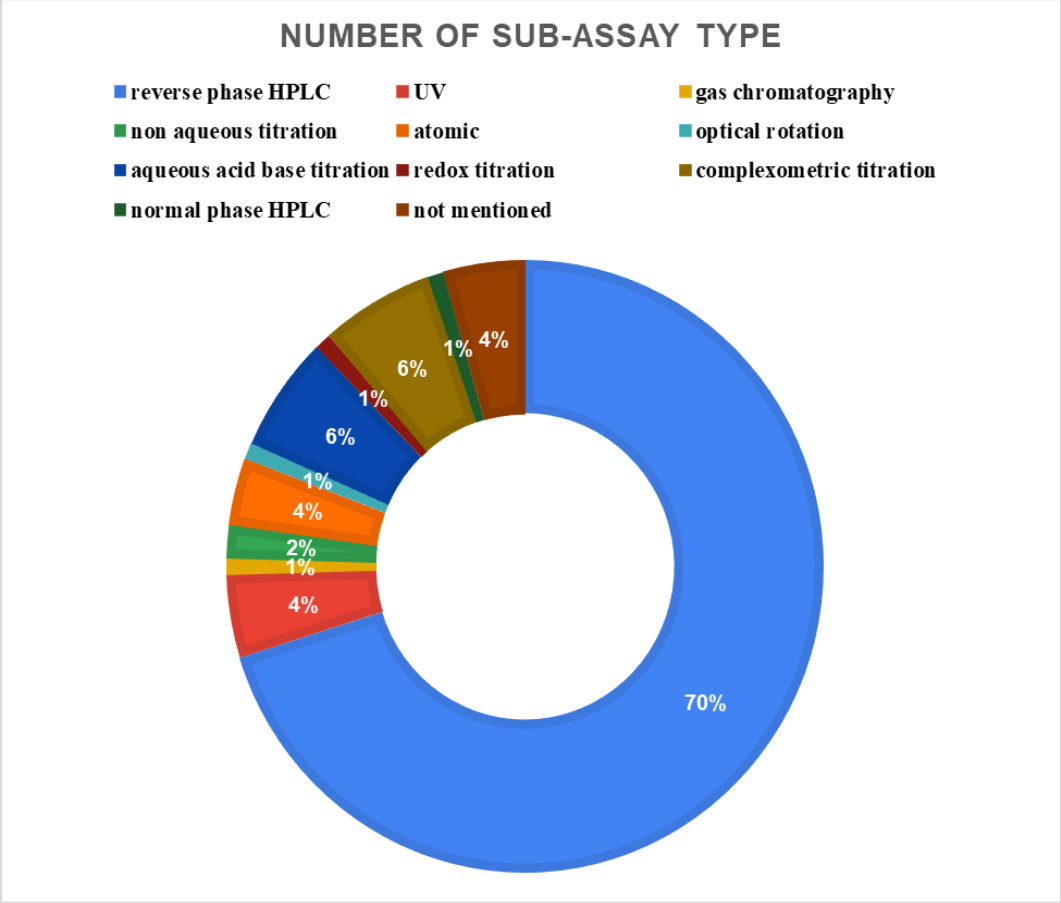

Figure1.2: Number of sub-assay type

3.2.1 Chromatographic sub assay

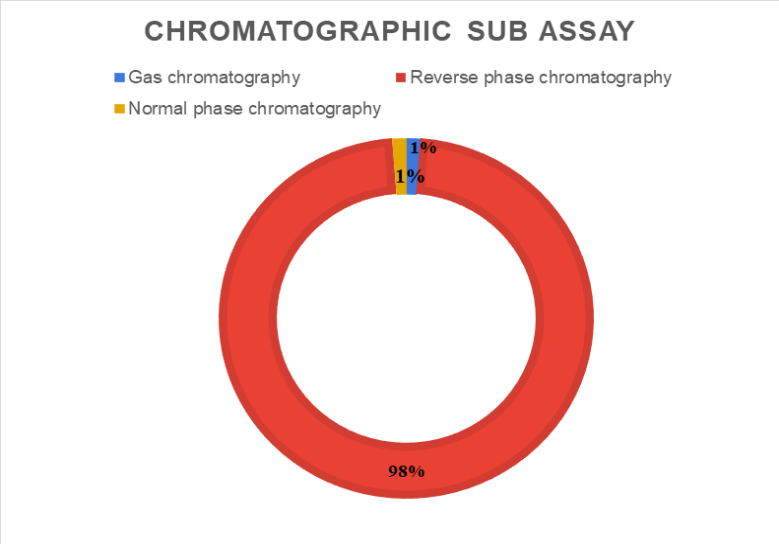

Figure 1.3: Chromatographic sub assay type

Due to its many benefits, reverse phase high performance liquid chromatography is widely used. The best method for analyzing hydrophobic pharmaceutical compounds is reverse phase HPLC. Because it successfully separates and holds these substances utilizing a nonpolar stationary phase, molecules. Due to its superior separation ability and resolution, reverse phase HPLC is a useful option for researching the creation of complex mixtures encountered in pharmaceutical substances. HPLC's reverse phase provides excellent sensitivity for exact quantification of drug content and unwanted component levels during pharmaceutical examination. This technique is incredibly adaptable; it allows for the accurate detection of drug compounds and boosts analytical power. (N'Cho, 2016)

On the other hand, there aren't many applications for normal phase HPLC and gas chromatography. The graph shows that it's only 1% for both techniques. The disadvantages of these-

Due to its polarity, normal phase HPLC has a limited use for hydrophobic molecules and is worthless for substances that firmly adsorb onto the stationary phase. It is also less sensitive

than reverse phase HPLC because of its separation and detection processes. Nonvolatile chemical applications for gas chromatography (GC) are constrained by potential temperature instability and compatibility with polar stationary phases.

3.2.2 Titrimetric sub assay type

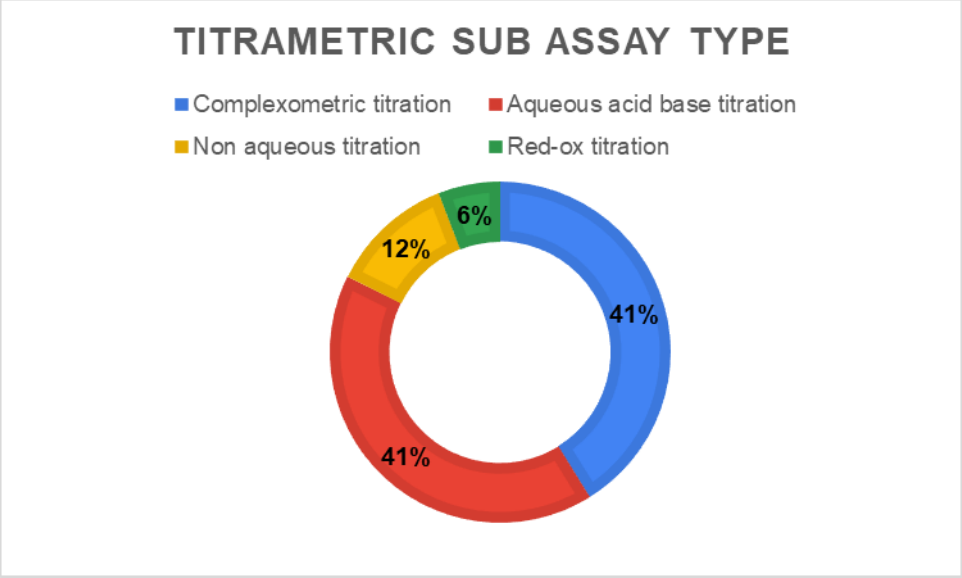

Figure 1.4: Titrimetric sub assay type

From the research we find out that out of 119 drug assays, 17 drugs are found which are assayed by titration based analysis. This is the second highest technique of this study. The presence of several subtypes of titration based analysis, such as aqueous acid base, redox, non-aqueous, and complexometric titrations, was then noted. Compared to chromatographic subtypes such, these approaches are extremely underutilized for several reasons.

Aqueous acid-base titrations cannot be used to test medications that are neither acidic nor basic due to their lack of specificity. Redox titrations are used for substances that undergo oxidation-reduction reactions, however they can only be utilized with substances that have specific redox properties. Potential impurity interference may reduce the validity of the results. Drugs that are

insoluble in water or chemicals with limited solubility in non-aqueous solvents should not be tested using non-aqueous titrations. They need to carefully choose solvents and titrants that work with the medicine. Only stable compounds can form stable complexes in complexometric titrations, and interference from other complexing agents or ligands can lead to inaccurate results (Caffrey, A. R., & Borrelli, E. P. , 2020)

3.2.3 Spectroscopic sub assay type

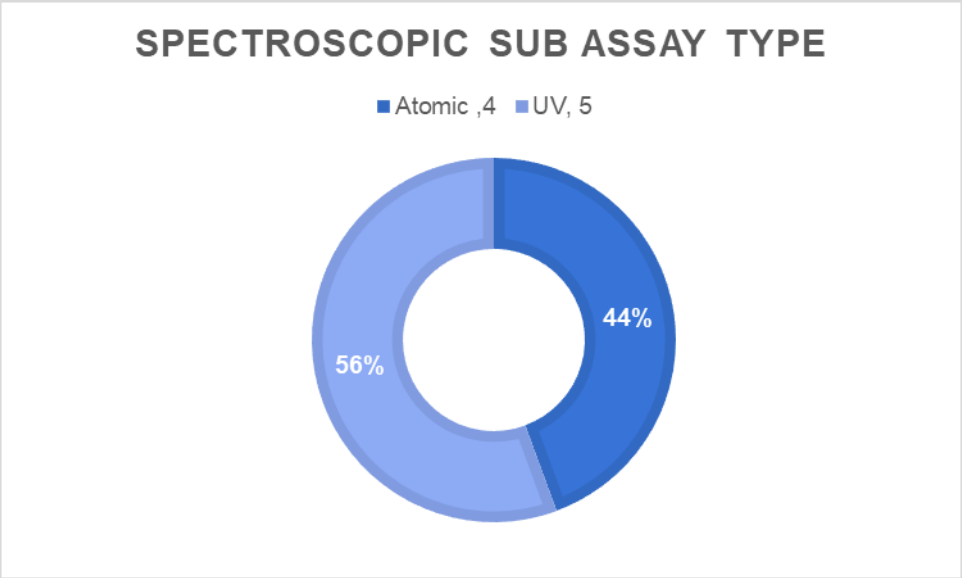

Figure1.5: Spectroscopic sub assay

UV and atomic spectroscopy are the next spectroscopic subtypes recommended by the BP for this study. Here, UV has been mostly used, and Five medications were recommended to be assayed for using UV spectroscopy. Only drugs with chromophores can be assayed by UV spectroscopy.

Atomic spectroscopy is nearly the same as UV, limited scope may be due to difficult sample preparation, a lack of chemical specificity, and decreased sensitivity in subtyping

investigations. The phases of digestion, extraction, or volatilization that are involved in sample preparation might be lengthy and could cause errors or sample losses. Atomic spectroscopy techniques might not be able to provide complex biological targets with rich subtype information or detect low-abundance subtypes with sufficient precision.

Chapter 4

Conclusion

The created database from this study did not provide conclusive results after analyzing the frequency of assay types and sub assay types utilized in drug quantitative assessment. The database only contains 119 of the 1247 formulas in BP. After incorporating all 1247 formulations found in BP, conclusive results would be produced. The completion of the database would be beneficial for students and teachers studying or analyzing the application of assay procedures. The created data base will also help to develop assay methods for newly founded drug. In future, a complete database can be constructed for all 1247 formulations.

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