CHAPTER-2

Literature survey & Experimental & Objectives
Section (i): DRUG PROFILE AND LITERATURE SURVEY

1. ATAZANAVIR

Atazanavir sulfate has the chemical name \((3S,8S,9S,12S)-3,12\)-Bis\((1,1\)-dimethylethyl\)-8hydroxy-4,11-dioxo-9-(phenyl methyl)-6-[4-(2pyridinyl)phenyl]methyl]-2,5,6,10,13penta aza tetra decanedioic acid dimethyl ester, sulfate \((1:1)\). It is a white to pale yellow crystalline powder with a molecular formula of \(C_{38}H_{52}N_6O_7\cdot H_2SO_4\) and a molecular weight of 802.9 g mol\(^{-1}\). The free base molecular weight is 704.9 g mole\(^{-1}\).

**Therapeutic importance**

Atazanavir sulfate is used in combination with other medications in controlling HIV infection, thereby improving the quality of life. It also lowers the risk of getting HIV disease complications (e.g. new infections, cancer). Atazanavir belongs to a class of drugs known as protease inhibitors.

**Therapeutic Category:** Antiviral.

The basic structure of the drug is as shown in Fig.2.i.1.

![Fig.2.i.1 Structure of atazanavir](image-url)
Atazanavir sulfate is an antiretroviral protease inhibitor used in the treatment of human immunodeficiency virus (HIV) Type-II and AIDS \(^{[1-2]}\). Literature survey indicated that few HPLC \(^{[3-12]}\) methods have been reported for its estimation from blood plasma, cerebrospinal fluid and blood serum. Few UV-Visible spectrophotometric \(^{[13-19]}\) methods also have been reported for the estimation of atazanavir sulfate in bulk and in pharmaceutical dosage forms.

Anindita Behera et.al\(^{[14]}\) have reported two simple and sensitive spectrophotometric methods for the determination of atazanavir sulphate in capsule dosage forms. The first method was based on the oxidative coupling of atazanavir with MBTH. The resultant green colored product showed \(\lambda_{\text{max}}\) at 627.3 nm and was stable for 2 hours. The second method was based on the diazotized reaction between the drug and N-(1-Napthyl) ethylene diamine dihydrochloride in neutral medium. The formed yellowish orange colored product showed \(\lambda_{\text{max}}\) at 517.1 nm. Beer’s law was obeyed in the concentration range of 10-120 and 1-10 \(\mu\)g mL\(^{-1}\) respectively.

P. Janakipathi et al \(^{[18]}\) have developed visible spectrophotometric methods for the estimation of atazanavir in pharmaceutical pharmulations. These methods are based on ion-association complexes formed between atazanavir and acid dyes i.e. Mordant Black-III or Solochrome Black-T. In these methods the formed ion-association complexes were extracted in to chloroform layer. The resultant colored chromogens showed absorption maximum at 537 nm and at 491 nm and Beer’s law was obeyed in the concentration range of 10-90 \(\mu\)g mL\(^{-1}\) and 1-12 \(\mu\)g mL\(^{-1}\) respectively.

K. Parameswara Rao et al \(^{[19]}\) reported two simple and sensitive extracted spectrophotometric methods for the determination of atazanavir using azo dyes i.e.
Tropeoline-OO (TPOOO) and Alizarine Red- S (ARS). The chloroform extracted layers showed $\lambda_{\text{max}}$ at 480 nm and 445 nm with molar absorptivity $5.126 \times 10^3 \text{ L mole}^{-1}\text{cm}^{-1}$ and $4.982 \times 10^3 \text{ L mole}^{-1}\text{cm}^{-1}$ respectively. For both methods, Beer’s law obeyed in the concentration range of 2.5-12.5 µg mL$^{-1}$.

As the analytical useful functional groups of atazanavir were not fully exploited and hence, the author had made an attempt to develop three simple and sensitive extractive spectrophotometric methods using acid dyes, i.e. bromothymol blue (BTB), bromophenol blue (BPB) and bromocresol green (BCG). Atazanavir forms yellow colored ion-association complexes with bromothymol blue (BTB), bromophenol blue (BPB) and bromocresol green (BCG) in phthalate buffer (pH-2.4). The resultant yellow colored solutions showed $\lambda_{\text{max}}$ at 414nm, 410nm and 417nm respectively. The colored solutions formed are highly sensitive and fairly stable.

2. EMTRICITABINE

Emtricitabine has the chemical name 4-amino-5-fluoro-1-[(2R,5S)-2-(hydroxymethyl)-1, 3-oxathiolan-5-yl]-1,2-dihydropyrimidin-2-one$^{[20]}$. It is white to off-white crystalline powder with a molecular formula of C$_{8}$H$_{10}$FN$_{3}$O$_{3}$S and a molecular weight of 247.24 g mole$^{-1}$.

Therapeutic Importance

Emtricitabine is a nucleoside reverse transcriptase inhibitor related to cytosine with antiretroviral activity against HIV. It is also active against Hepatitis-B virus.It is used with other antiretroviral for combination therapy of HIV infection.

**Therapeutic Category:** Anti viral.
The basic structure of the drug is as shown in Fig.2.i.2

![Chemical Structure of Emtricitabine](image)

**Fig.2.i.2. Structure of emtricitabine**

Emtricitabine works by inhibiting reverse transcriptase enzyme that copies HIV RNA into new viral DNA. It can help lower the level of HIV in the patient’s body and can indirectly increase the number of immune system cells (called T cells or CD$_{4+}$ T-cells). It is used for the prevention of perinatal HIV-1 reverse transcriptase $^{[21]}$. It is also active against Hepatitis-B-virus $^{[22, 23]}$. Literature survey indicated that few analytical methods are reported for the analysis of emtricitabine by HPLC $^{[24]}$, LC $^{[25]}$, HPLC-in plasma $^{[26-29]}$, HPTLC $^{[30]}$ and few UV-spectrophotometric methods $^{[31-36]}$ either alone or combined with other drugs. To the best of our knowledge, only one visible spectrophotometric method was reported by Janakipathi et al $^{[37]}$.

Nagaraju P.T et al $^{[32]}$ developed two simple, precise and economical methods for the estimation of emtricitabine in bulk and in pharmaceutical formulations. In first method emtricitabine has the absorbance maxima at 241.1 nm in methanol as solvent. In second method, the first order derivative spectrum showed zero crossing at 241.1 nm, with a sharp peak at 232.7 nm. In both methods, Beer-Lambert’s law obeyed in the concentration range 5-30 µg mL$^{-1}$. 
C.M. Bhaskar Reddy et al\textsuperscript{[33]} reported simple UV spectrophotometric determination of emtricitabine in pure and in its pharmaceutical formulations. In this method, methanol was used as solvent. The drug exhibited absorption maximum at 420 nm with apparent molar absorptivity of $7.23 \times 10^4$ L mole\(^{-1}\) cm\(^{-1}\). Beer’s law is obeyed in the concentration range of 2.0-18.0 µg mL\(^{-1}\).

Mohammad H. Abdel Hay et al\textsuperscript{[34]} reported simple spectrophotometric methods for the determination of tenofovir fumarate and emtricitabine in bulk powder and in tablets. In this method high purified water was taken as solvent. The first method involved the application of first derivative spectrophotometry involving measurement at 298.5 nm for the determination of emtricitabine in the presence of tenofovir.

P.Janaki pathi et al\textsuperscript{[37]} developed three visible spectrophotometric methods for the estimation of emtricitabine in pharmaceutical formulations. The first method is based on formation of Schiff’s base complex between the drug and PDAC in the presence of sulphuric acid with λ\(_{\text{max}}\) at 538 nm and with a molar absorptivity $2.8 \times 10^3$ L mole\(^{-1}\) cm\(^{-1}\). In the second method, the drug was treated with MBTH in the presence of ceric ammonium sulphate by oxidative coupling reaction forming bluish green colored solution with λ\(_{\text{max}}\) at 635 nm and with molar absorptivity $1.86 \times 10^4$ L mole\(^{-1}\) cm\(^{-1}\). The third method is based on ion-association complex formed between emtricitabine and mordant black-III in the presence of potassium hydrogen phthalate buffer (pH 2.4). which shows the maximum absorbance at 543 nm. Beer’s law was obeyed in the concentration range 10-90 µg mL\(^{-1}\) with molar absorptivity of $1.87 \times 10^3$ L mole\(^{-1}\) cm\(^{-1}\).
In the present investigations the author has attempted to develop three simple, sensitive, accurate and economical visible spectrophotometric methods for the determination of emtricitabine in bulk and in its pharmaceutical formulations using \( p \)-dimethylaminobenzaldehyde (PDAB), 3-Methyl-2-benzothiazolinonehydrazone (MBTH) and 4-Hydroxy-3-methoxybenzaldehyde (HMBA) as chromogenic reagents.

3. EPLERENONE

Eplerenone has the chemical name Pregn-4-ene-7, 21-dicarboxylic acid, 9, 11-epoxy-17-hydroxy-3-oxo,\( \gamma \)-lactone,methyl ester \( (7\alpha, 11\alpha, 17\alpha) \). It is a off-white, crystalline powder with a molecular formula of \( \text{C}_{24}\text{H}_{30}\text{O}_{6} \) and a molecular weight of 414.50 g mole\(^{-1}\).

**Therapeutic importance**

Eplerenone is a potassium-sparing diuretic, meaning that it helps the body get rid of water but still keep potassium. Eplerenone is used specifically for the reduction of risk of cardiovascular death in people with heart failure and left ventricular dysfunction within 3-14 days of an acute myocardial infarction, in combination with standard therapies and as treatment against hypertension. Eplerenone is used alone or in combination with other medicines to treat high blood pressure. It is used in treatment of hypertension and it is used as an adjunct in the management of chronic heart failure.

**Therapeutic Category:** Anti hypertensive and diuretic.

The structural formula is as shown in Fig.2.i.3.
Eplerenone is an aldosterone antagonist used as an adjunct in the management of chronic heart failure \cite{38-40}. It is clinically used as antihypertensive and diuretic. Literature survey indicated that LC-MS methods have been reported for its estimation from human plasma and urine.\cite{41, 42} Two spectrophotometric methods have been reported for the estimation of eplerenone in bulk and pharmaceutical dosage forms\cite{43, 44}.

V.S. Banode et.al\cite{43} reported UV-Spectrophotometric method for the estimation of eplerenone in bulk drug and tablets. In this method absorbance maximum was showed at 242.5 nm in methanol and water (80:20) as mixed solvent. Beer’s law was obeyed in the range of 0-45 µg mL\(^{-1}\). The reported method was validated as per the ICH and USP guidelines.

A.L. Ganure et al\cite{44} developed spectrophotometric method for the determination of eplerenone. In this method the keto group of eplerenone was condensed with 2,4-dinitrophenyl hydrazine to gives orange colored hydrazone complex in the presence of 0.1N H\(_2\)SO\(_4\). The obtained colored chromogen showed \(\lambda_{\text{max}}\) at 430 nm with molar absorptivity \(3.177 \times 10^4\) L mole\(^{-1}\)cm\(^{-1}\). Beer’s law was obeyed in the concentration range 5-35 µg mL\(^{-1}\).
In the present study, the author describes three simple, sensitive and economical extractive spectrophotometric methods for the estimation of eplerenone in tablet dosage forms.

4. OLOPATADINE

Olopatadine has the chemical name \((11Z)-11-[3-(\text{dimethyl amino})\text{ propylidene}]\)-6, 11-dihydrodibenzo \([b, e]\) oxepin-2-yl\} acetic acid. It is a white, crystalline powder with a molecular formula of \(C_{21}H_{23}NO_3\) and a molecular weight of \(337.412\) g mole\(^{-1}\).

**Therapeutic importance**

Olopatadine tablets are prescribed for the treatment of allergic rhinitis, urticaria and itching accompanied by skin diseases, i.e. eczema, dermatitis, pruritus, cutaneous, psoriasis vulgarism and erythematic exudativum multiforms.

**Therapeutic Category:** Anti-allergic, anti-asthmatic and anti-arthritic.

The structural formula is as shown in Fig.2.i.4.

![Fig.2.i.4. Structure of Olopatadine](image-url)
Olopatadine is an antihistamine and mast cell stabilizer. It is a selective inhibitor for the release of histamine and other pro-inflammatory mediators from the mast cell \(^{45}\). Olopatadine is a potent, selective histamine H\(_1\) antagonist that inhibits the in vivo type 1 immediate hypersensitivity reaction. Literature survey reveals that estimation of olopatadine was reported by using HPTLC\&HPLC\(^{46,47}\), and RP-HPLC\(^{48}\) methods. Several LC-MS methods have been reported for the estimation of olopatadine hydrochloride in human plasma\(^{49-51}\) and a UV-Spectrophotometric\(^{52}\) method has been reported for the validation and estimation of olopatadine.

Suddhasattyadey et.al\(^{52}\) have reported method development and validation for the estimation of olopatadine in bulk and pharmaceutical dosage forms and its stress degradation studies using UV spectrophotometric method. In this method, the absorption maximum for olopatadine has noticed at \(\lambda_{max}\) at 206nm in methanol and 0.1NHCl (50:50) as solvent. Beer’s law was obeyed in the concentration range 2-10 \(\mu\text{g mL}^{-1}\) with molar extinction coefficient 9.86x \(10^{2}\) L mole\(^{-1}\) cm\(^{-1}\).

Literature survey indicated that no visible spectrophotometric method was reported for the determination of olopatadine at the time of the author intended the research. Hence, the present author has developed three simple, sensitive and economical visible spectrophotometric methods for the estimation of olopatadine using acid dyes i.e. bromothymol blue (BTB), bromophenol blue (BPB) and bromocresol green (BCG) in tablet dosage forms.
5. PEMETREXED DISODIUM

Pemetrexed disodium hepta hydrate has the chemical name L- Glutamic acid, N-[4-[2-(2-amino-4,7-dihydro-4-oxo1H-pyrrolo[2,3-d]pyrimidin-5-yl)ethyl] benzoyl]-disodium salt heptahydrate\[^{[53]}\], with a molecular formula of C\(_{20}\)H\(_{19}\)N\(_5\)O\(_6\).7H\(_2\)O and a molecular weight of 597.49 g mole\(^{-1}\).

**Therapeutic importance**

Pemetrexed is used in combination with cisplatin therapy for the initial treatment of patients with locally advanced or metastatic nonsquamous non-small cell lung cancer. Pemetrexed is indicated for the maintenance treatment of patients with lung cancer whose disease has not progressed after four cycles of platinum-based first-line chemotherapy. It is also prescribed as a single-agent for the treatment of lung cancer after prior chemotherapy. In combination with cisplatin it is used in the treatment of patients with malignant pleural mesothelioma whose disease is unrespectable or who are otherwise not candidates for curative surgery.

**Therapeutic Category:** Anticancer.

The basic structure of the drug is as shown in Fig.2.i.5.

![Fig.2.i.5. Structure of pemetrexed disodium](image-url)
Pemetrexed (Alimta; Eli Lilly, Indianapolis, IN) is a folate anti metabolite that primarily inhibits thymidylate synthase. Pemetrexed shows activity against a variety of solid tumor in clinical trials, that is non-small-cell lung and breast cancers. It also inhibits both dihydrofolate reductase and glycaminide ribonucleotide formyl transferase. Literature survey indicated that few analytical methods have been reported for the determination of pemetrexed disodium such as HPLC, RP-HPLC and LC methods. Few spectrophotometric methods were also reported for its validation in drug samples.

Ankit D. Patel et al reported HPLC and UV spectrophotometric methods for the estimation of pemetrexed disodium in bulk and pharmaceutical formulations. In UV spectrophotometric method the drug showed an absorbance maximum at 225 nm with distilled water as solvent. Beer’s law was obeyed in the concentration range 2-16 µg mL⁻¹ with molar absorptivity 3.39 x 10⁴ L mole⁻¹ cm⁻¹.

P.Jankipathi et al developed three visible spectrophotometric methods for the estimation of pemetrexed disodium in pharmaceutical formulations. In the first method the drug formed orange-red colored chromogen with 1,2-Napthoquinone-4-sulphonic acid(NQS) in basic medium which showed λ_max at 495 nm. Beer’s law was obeyed in the limits of concentration of 10-80 µg mL⁻¹ with molar absorptivity 3.77x 10⁴ L mole⁻¹ cm⁻¹. The second method was based on the oxidative coupling reaction between MBTH and the drug in the presence of ferric chloride forming green colored chromogen with λ_max at 735 nm with molar absorptivity 6.65 x10⁴ L mole⁻¹ cm⁻¹. The third method was based on formation of Schiff’s base complex between the primary amine group of the drug and the aldehyde group of PDAB, forming reddish colored complex showing maximum
absorbance at 505 nm. The three methods were applied for the determination of pemetrexed disodium in parenteral formulations.

In the present study, we are reporting three simple, sensitive, accurate and economical spectrophotometric methods for the determination of pemetrexed disodium in bulk and pharmaceutical formulations using $p$-Dimethylaminocinnamaldehyde (PDAC), 4-Hydroxy-3-methoxybenzaldehyde (HMBA) and 3-Methyl 2-benzothiazolinone hydrazone (MBTH) as chromogenic reagents.

6. ZOLMITRIPTAN

Zolmitriptan has the chemical name (4S)-4-([3-[2-(Dimethyl amino) ethyl]-1H-indol-5-yl] methyl)-1,3-oxazolidin-2-one with molecular formula $C_{16}H_{21}N_{3}O_{2}$ and molecular weight of 287.35 g mole$^{-1}$.

**Therapeutic importance**

Zolmitriptan is used for the acute treatment of migraines with or without aura in adults. Zolmitriptan is not intended to the prophylactic therapy of migraine or use in the management of hemiplegic or basilar migraine.

Zolmitriptan is available as a swallowable tablet, an oral disintegrating tablet and as a nasal spray, in doses of 2.5 and 5.0 mg. people who get migraines from aspartame should not use the disintegrating tablets (Zomig ZMT), which contain aspartame.

**Therapeutic Category:** Anti-migraine

The basic structure of the drug is as shown in Fig.2.i.6.
Zolmitriptan belongs to a group of medicines known as serotonin 5-HT1D receptor agonists. It works by stimulating serotonin receptor in the brain. Literature survey indicated that few analytical methods have been reported for the analysis of zolmitriptan. They include some HPLC methods associated with coulometric \cite{66}, mass spectrometry \cite{67-69} and photometric \cite{70-78} detectors. Other methods such as UPLC \cite{79}, voltammetric \cite{80}, Liquid chromatography-Mass spectrometry \cite{81} and UV-Visible spectrophotometric methods \cite{82-90} are also reported.

Syeda Humaira et al \cite{83} have been developed simple, sensitive, economical UV-spectrophotometric method for the determination of zolmitriptan in tablet formulations. Zolmitriptan shows absorption maximum at 226.5 nm in ethanol as solvent. Beer’s law was obeyed in the concentration range 1-5 µg mL\(^{-1}\) with molar absorptivity \(7.7 \times 10^4\) L mole\(^{-1}\) cm\(^{-1}\).

Asad Raza et al \cite{86} developed a novel spectrophotometric method for the determination of zolmitriptan in pharmaceutical formulations. The method is based on the charge- transfer between zolmitriptan and 2,3-dichloro-5,6-dicyano1,4-benzoquinone (DDQ) to form color product which shows maximum absorbance at 555 nm. The molar ratio of the complex formed between ZOL and DDQ reagent was investigated as 1:1.
Beer’s law is obeyed in the concentration range 10-250 µg mL\(^{-1}\) with molar absorptivity 1.7 x 10\(^3\) L mole\(^{-1}\) cm\(^{-1}\).

Ayman.A. Gouda et al\(^{[88]}\) reported a facile, accurate, sensitive and validated spectrophotometric method for the determination of zolmitriptan in pure and dosage forms. These methods are developed by using charge-transfer reaction between the drug and various charge complexing reagents i.e. 7, 7, 8, 8, - tetra cyano quinodimethane (TCNQ), P-chloranilic acid (P-CLA), Quinalizarine (QUIZ) and Alizarin Red-S (ARS) producing charged complexes. The formed colored chromogens quantitatively showed \(\lambda_{max}\) at 840 nm, 532nm, 554 nm and 534 nm respectively. Beer’s law was obeyed in the concentration range 3-30 µg mL\(^{-1}\), 10-140 µg mL\(^{-1}\), 2-20 µg mL\(^{-1}\), and 1-10 µg mL\(^{-1}\) with molar absorptivities 1.045x 10\(^4\) L mole\(^{-1}\)cm\(^{-1}\), 0.729x 10\(^4\) L mole\(^{-1}\)cm\(^{-1}\), 1.286x 10\(^4\) L mole\(^{-1}\)cm\(^{-1}\) and 2.008x10\(^4\) L mole\(^{-1}\)cm\(^{-1}\) respectively.

K.N.Prashanth et al\(^{[89]}\) developed an accurate and precise spectrophotometric method for the estimation of zolmitriptan using vanillin as reagent. The method is based on the formation of enamine between the secondary amino group of zolmitriptan and aldehyde group vanillin. The formed colored product shows maximum absorbance at 580 nm with molar absorptivity 3.3x10\(^3\) L mole\(^{-1}\)cm\(^{-1}\) and Sandell’s sensitivity 0.0872 µg cm\(^{-2}\).

T. Mohamood Ansari et al\(^{[90]}\) reported a fast and selective spectrophotometric method for the determination of zolmitriptan in bulk and dosages forms. The method is based on the formation of blue colored chromogens due to the reduction of tugstate ion in Folin-Ciocalteu reagent by zolmitriptan in alkaline medium. The colored species has...
showed the absorption maximum at 750 nm and Beer’s law was obeyed over the concentration range 3-50 µg mL\(^{-1}\).

The survey of literature indicated that, very few visible spectrophotometric methods for the analysis of zolmitriptan were reported at the time of the commencement of this investigation. In the present investigation the author is reporting simple, sensitive and industry friendly spectrophotometric methods for the determination of zolmitriptan using PDAC, PDAB and NQS. The secondary amine of the cyclic imine group in the indole portion of the drug reacts with the above said reagents forming intense colored species whose absorbance was measured spectrophotometrically.
Section (ii): Reagents and instruments employed in the present investigations

a) Instruments used

Shimadzu UV-1700 Pharma spec with 1cm matched quartz cell was used for spectral measurements.

b) pH meter

A Digi sun digital pH meter was used for pH measurements.

b) Preparation of reagents

All the chemicals and reagents used were of analytical grade and the solutions were prepared in double distilled water.

1) Bromothymol blue (0.2% w/v)

200mg of bromothymol blue was dissolved in a mixture of 8.0mL NaOH (0.02N) and 25.0mL ethanol (95%). The solution was then made up to 100mL with distilled water.

2) Bromophenol blue (0.2% w/v)

200mg of bromophenol blue was dissolved in a mixture of 8.0mL NaOH (0.02N) and 25.0mL ethanol (95%). The solution was then made up to 100mL with distilled water.
3) Bromocresol green (0.2% w/v)

200mg of bromo cresol green was dissolved in a mixture of 8.0mL NaOH (0.02N) and 25.0mL ethanol (95%). The solution was then made up to 100mL with distilled water.

4) \( p \)-Dimethylamino benzaldehyde (5.0% w/v)

Accurately weighed 5.0 g of \( p \)-dimethylaminobenzaldehyde and dissolved in methanol and made up to the mark with methanol in 100 mL volumetric flask.

5) \( p \)-Dimethylamino cinnamaldehyde (5.0% w/v)

5.0 g of \( p \)-Dimethylaminocinnamaldehyde were weighed and dissolved in methanol and diluted to 100 mL with methanol in volumetric flask.

6) 4-Hydroxy-3-methoxybenzaldehyde (HMBA) (5.0 % w/v)

5.0 g of 4-Hydroxy-3-methoxybenzaldehyde (HMBA) were dissolved in 100 mL of methanol in volumetric flask.

7) MBTH (0.1% w/v)

100mg of 3-Methyl 2-benzothiazolinone hydrazone were dissolved in distilled water and made up to the mark with distilled water in 100 mL volumetric flask.

8) 1, 2-Napthaquinone -4- sulphonic acid (NQS) (0.5% w/v)

This solution was prepared by dissolving 500mg of reagent in 100mL distilled water.
9) Potassium hydrogen phthalate buffer (pH-2.4)

4.1gm of potassium hydrogen phthalate were dissolved in 100mL of distilled water. To 25mL of this solution, 21.0mL of 0.2M HCl were added and diluted to 100mL with distilled water to obtain a buffer solution of pH-2.4.

10) FeCl₃ (0.1% w/v)

100mg of ferric chloride were dissolved in water and made up with distilled water in 100 mL volumetric flask.

11) Cerric ammonium sulfate (0.5% w/v)

250 mg of cerric ammonium sulfate were dissolved in 50 mL volumetric flask with distilled water and diluted the volume with distilled water.

12) Sulphuric acid (0.1N)

0.27 mL of concentrated sulphuric acid was diluted to 100mL with distilled water in a 100mL beaker and standardize volumetrically.

13) Sodium hydroxide (0.01N)

40mg of anhydrous sodium hydroxide were dissolved in 100mL distilled water.
Section (iii): Objectives of the present investigations

Quality is important in every product or service and it is vital in medicine as it involves saving of life. Unlike ordinary consumer goods, there should not be and there is no “second” quality in drugs. Quality control is a concept, which strives to produce a perfect product by a series of measures designed to prevent and eliminate errors at different stages of production. As a matter of fact, it is built in from the time of inception of the thought to make a product, to the time it is finally made and sent out with an OK quality report.

In popular practice, the quality of medicines or pharmaceutical products is assured through quality control. It is, therefore, essential that quality assurance department must adopt “Good Laboratory Practice” to ensure reliability of pharmaceuticals together with their careful control which are our moral obligations arising from the humanism towards sick human beings. Consequently, the manufacturing and the control of drugs are very responsible and they need substantial knowledge of the science. The decision to release or reject a product is based upon one or two types of control actions or combination of both. If the product is a single entity of high purity, the analytical data is the basis for decision but most of the time the formulation is a physical mixture of several potent drugs. With the growth of pharmaceutical analysis involving complex instrumentations, providing simple analytical procedures for complex formulations has become a matter of foremost importance.

Drugs and pharmaceuticals play a very significant role today for prevention, control and curing of different kinds of human diseases. It is a common observation and the practical truth that a single drug of a particular composition is marketed in various
brand names by different manufacturers. The possibility of minor changes in the chemical composition and standard of the drug will have a profound effect on the physiological and biological activities of the patient. It is very much painful for the present day scientist in general and to the analytical pharmaceutical chemist in particular to note in the various dailies about the entry of spurious and substandard drugs into market, which definitely will have an adverse effect on the human beings at large.

SELECTED DRUGS FOR THE PRESENT STUDY

The main goal of the present work is to develop various sensitive and selective analytical methods, employing easily available chemicals and cost effective techniques such as UV-Visible spectrophotometry for the determination of six pharmaceutical drugs useful in the treatment of viral, cancer, allergic, asthma, and migraine diseases.

In visible spectrophotometry, the reactions carried out were selected purely based on the availability of the functional groups in the drug under investigation. The presence of diverse functional groups and other oxidizing or reducing sites in the drugs investigated offered reactions for their assay. Ion-pair, condensation, electrophilic coupling and derivatize complexation reactions were used as basis for the methods that were developed for the selected drugs. In each case, based on the reaction stoichiometry between the drug and reactant or background literature, tentative reaction schemes have been proposed.

For each and every reaction, various experimental conditions like acid or base concentration, pH, reaction time, reagent concentration, the evaluation of linear range, limits of detection, limits of quantification, regression equation were studied and optimized.
1. Atazanavir:

   Atazanavir is an azapeptide HIV-1 protease inhibitor (PI). It is a protease inhibitor with activity against Human Immunodeficiency Virus Type 1 (HIV-1). Atazanavir sulphate, the first once-daily HIV-1 protease inhibitor was approved by the US FDA for the treatment of HIV-1 infection in combination with other antiretroviral agents.

2. Emtricitabine:

   Emtricitabine is an analogue of cytidine. It works by inhibiting reverse transcriptase, the enzyme that copies HIV RNA into new viral DNA. It is a Nucleoside Reverse Transcriptase Inhibitor (NRTI) for the treatment of HIV infection in adults and children.

3. Eplerenone:

   Eplerenone is a competitive antagonist of the aldosterone receptor. It binds to the mineralocorticoid receptor and blocks the binding of aldosterone. It is used in treatment of hypertension and as an adjunct in the management of chronic heart failure.

4. Olopatadine:

   Olopatadine is an antihistamine, anti cholinergic and mast cell stabilizer. It is used as inhalers to treat asthma, as nasal sprays to treat hay fever (allergic rhinitis) and as eye drops for allergic conjunctivitis. Finally in oral form they are used to treat the rare condition of mastocytosis.

5. Pemetrexed disodium:

   Pemetrexed disodium is a drug that belongs to a class of chemotherapeutic drugs known as folate anti metabolites. Pemetrexed is an antifolate, a substance that blocks the activity of folic acid. Pemetrexed is used in treatment of some form of lung cancer and in
treatment of mesothelioma. It is used in combination with cisplatin is indicated for the treatment of patients with malignant pleural mesothelioma whose disease is unrespectable or who are otherwise not candidates for curative surgery.

6. Zolmitriptan:

Zolmitriptan is a selective 5-Hydroxytryptamine type 1B and 1D, \(5\text{-HT}_{1\text{B/1D}}\) receptor agonist. Zolmitriptan binds with high affinity to human recombinant \(5\text{-HT}_{1\text{B}}\) and \(5\text{-HT}_{1\text{D}}\) receptors leading to cranial blood vessel constriction. Zolmitriptan is used for the acute treatment of migraines with or without aura in adults.

It is with this challenge in mind; the author has taken up thorough investigations to evaluate the purity of the various drugs released into the market. The author has made an extensive survey of the chemical and biochemical literature to know whether the reports involving simple experimental techniques such as the spectrophotometric techniques are available for ascertaining the assay and purity of the drugs. It is the observation of the author that not much attention is paid to simple and rapid spectrophotometric methods for the assay of the above selected drugs available in literature. Various instrumental techniques (HPLC, GC, Fluorimetry, NMR, IR, UV and Visible regions) are available in literature for the assay of the selected drugs. These methods are either expensive or are not reproducible.

Spectrophotometry is considered the most convenient analytical technique due to its inherent simplicity, low cost and wide availability in most quality control and clinical laboratories. The selectivity and sensitivity of the spectrophotometric methods depend only on the nature of chemical reactions involved in color development and not on the sophistications of the experiment.
Visible spectrophotometry may serve as useful alternatives to many of the aforesaid sophisticated techniques because of their cost-effectiveness, ease of operation, sensitivity, remarkable accuracy and precision and wide applicability. UV and visible spectrophotometric methods are highly versatile, sensitive and reproducible. This made the author to develop new spectrophotometric methods for the estimation of some selected drugs having uses in pharmaceutical preparations.
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