Chapter-2
Survey of literature and objectives of the present investigation
(a). Cisapride:

Various methods are reported for the estimation of cisapride such as colorimetric method\textsuperscript{1,2}, spectrophotometric method\textsuperscript{3--9}, spectrophotometric and HPLC method\textsuperscript{10}, HPLC method\textsuperscript{11-17} and liquid chromatographic (LC) method\textsuperscript{18}.

Parimo et al\textsuperscript{1}, proposed a method for the determination of cisapride in dosage forms by colorimetric. This method is based on the reaction of cisapride with p-dimethyl amino cinnamaldehyde (PDAC) in presence of trichloroacetic acid in presence of methanol to form a very stable red schiff's base which has a $\lambda_{\text{max}}$ at 525 nm and obey Berr's – Lambert law in the range concentration of 50-10 mg/ml.

Krishna kumar, K.R and R.Raju\textsuperscript{2}, proposed a colorometric method for the estimation of cisapride and its dosage forms. This method is based on the diazotisation of cisapride with HCl and NaNO\textsubscript{2} and then coupled with 1-naphthyl ethylenediamine to give a red complex. The maximum absorbance is recorded at 539 nm. Beer’s law was obeyed over a concentration range of 1 to 11 mg/ml.

S.P.Vyas etal\textsuperscript{3}, proposed a simple UV. Spectrophotometric method for the determination of cisapride in pharmaceutical dosage forms. In this method, cisapride is dissolved in DMF to give a clear solution having $\lambda_{\text{max}}$
at 274.4 nm. The solution obeyed Beer’s law in the concentration range 2 to 20 mg/ml.

Revanasiddappa, H.D et al\textsuperscript{4}, have developed Spectrophotometric method for determination of some therapeutic agents using acetyl acetone. Suitable portions of standard drug solutions were diazotized with 2 ml of 0.1% sodium nitrite solution and 1 ml 1M-hydrochloric acid solution. After 3 minute, unconsumed nitrous acid was removed with 1 ml of 3% sulfamic acid. Portions (4 ml) of 5% acetylacetone and 4 ml of 4M NaOH were added and the solutions were diluted to 25 ml with methanol. The absorbances of the diluted solution were measured at 460, 445, 430 and 430 nm for dapsone, cisapride, metoclopramide and p-aminobenzoic acid, respectively.

Barbhai, A.J et al\textsuperscript{5}, proposed a Spectrophotometric estimation of cisapride using para dimethyl amino cinnamaldehyde and ortho phosphoric acid. The described spectrophotometric procedure was based on the reaction of cisapride with p-dimethyl amino cinnamaldehyde and ortho phosphoric acid. For preparation of a calibration curve, a stock solution of 1 mg/ml of cisapride in methanol was prepared. Powdered tablets equivalent to 50 mg cisapride were extracted with methanol and filtered. Measured volumes of the standard solutions were placed in 10 ml volumetric flasks and
methanolic solutions of 2 ml 0.1% p- dimethyl amino cinnamaldehyde and 2 ml 50% ortho phosphoric acid were added. The flasks were shaken for 1 min and made up to the mark with methanol. The absorbance was measured after 15 min at 546.5 nm. The sample solutions were measured similarly. The orange colour was stable for at least 2 h and Beer's law was obeyed from 160-650 µg/ml. The standard deviation was +/-0.04988256, the coefficient of variation +/-0.49811 and recoveries were 98-100.7%.

Sastry, C.S.P etal\textsuperscript{6}, proposed a new visible Spectrophotometric method for the Assay of cisapride in pharmaceutical formulations. Pharmaceuticals in CHCl\textsubscript{3} or aqueous acetic acid solutions (preparation described) were: (i) diluted to 4 ml with H\textsubscript{2}O, mixed with 2 ml 3-methyl-2-benzothioazolinone hydrazone hydrochloride and 1.5 ml Fe(III), the mixtures diluted to 8.5 ml with H\textsubscript{2}O, equilibrated for 40 min and then diluted to 25 ml prior to measurement of absorbance at 565 nm; (ii) mixed with 1.5 ml Fe(III) in 1M HCl and 2 ml 1,10-phenanthroline, the mixtures diluted to 10 ml with H\textsubscript{2}O, heated in a boiling-water bath for 30 min, cooled to room temperature, mixed with 2 ml H\textsubscript{3}PO\textsubscript{4}, diluted to 25 ml with H\textsubscript{2}O and equilibrated for 5 min prior to measurement of absorbance at 520 nm; or (iii) mixed with 0.5 ml chloranilic acid in CHCl\textsubscript{3}/propan-2-ol (4:1) and diluted to 10 ml with CHCl\textsubscript{3} prior to measurement of absorbance at 555 nm. For the
three methods, respectively, Beer's law was obeyed from 2-32, 0.4-6.4 and 25-450 μg/ml cisapride, absorptivities were 14 300, 63 000 and 1030, and the RSD (n = 6) were 0.54%, 0.33% and 0.76%. Recoveries were 98.9-101.9%. The effects of interferents were investigated.

Sastry, C.S.P et al., have developed a simple spectrophotometric method for estimation of cisapride in pharmaceutical formulations. Sample equivalent to 100 mg cisapride (I) was extracted with 3 x 20 ml CHCl₃, filtered and the extract was diluted to 100 ml with CHCl₃. Portions were analysed with use of 0.2% Suprachen Violet 3B, 0.4% Erioglaucine A, 0.2% Naphthalene Blue 12 BR or 0.2% Tropaeolin (methods A, B, C and D, respectively). For methods A and B, sample was mixed with glycine hydrochloride buffer of pH 1.3 (buffer A) and dye solution, the organic phase was dried over anhydrous Na₂SO₄ and the absorbance was measured at 595 and 640 nm, respectively. For methods C and D sample was mixed with buffer A of pH 1.5 (method C) or 0.1M-HCl (method D) and dye solution, the organic phase was dried over Na₂SO₄ and the absorbance was measured at 620 and 500 nm, respectively.

Meena, S et al., have developed an extractive photometric method for determination of cisapride. A standard solution of cisapride was mixed with
mentanil yellow (0.025% w/v) in pH 2.4 buffer. The resulting ion-pair was extracted in CHCl₃. The absorbance of the organic layer was measured on a Shimadzu UV spectrophotometer-1201 at 408 nm. The calibration graph was linear from 4-16 μg/ml. The recovery was 98.5-100.2%.

Hassan, E.M et al⁹, have developed derivative spectrophotometric and high performance liquid chromatographic methods (HPLC) for the determination of cisapride in pharmaceutical preparations. Spectrophotometrically, cisapride was determined by measuring the 1D-values at 264, 300 nm and 2D-values at 276, 290 and 276-290 nm. Beer's Law was obeyed in the range 2-12 μg/ml. The HPLC method depends upon using micropack-Si-10 column at ambient temperature with a mobile phase consisting of methanol-concentrated ammonia (99.25:0.75) at a flow rate of 1 ml/minute. Quantization was achieved by UV detection at 272 nm using quinine as internal standard. Calibration curve was linear over the concentration range 2-10 μg/ml. Both derivative spectrophotometry and HPLC methods showed good linearity, precision and reproducibility. No interference was found from tablet or suspension matrices at the selected derivative wavelengths and chromatographic conditions. The proposed methods were successfully applied to the assay of commercial tablets and

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suspension. The procedures were rapid, simple and suitable for quality control applications.

(b). Sulfamoxole:

Various techniques adopted for the estimation of Sulfamoxole are Spectrophotometric method\textsuperscript{19}, Colorimetric method\textsuperscript{20} and HPLC method\textsuperscript{21,22} Raghuveer, S et al\textsuperscript{19}, proposed a sensitive and rapid colorimetric method for the determination of sulfamoxole in its dosage forms. The method was based on the reaction of the drug with 4-dimethylamino cinnamaldehyde in the presence of orthophosphoric acid in methanolic medium. The red coloured chromogen had an absorption maximum at 545 nm.

Rami Reddy and I.E.Chakravarthy\textsuperscript{20}, proposed a simple spectrophotometric estimation of sulfamoxole in pharmaceutical formulations. In this method the drug treated with sodium nitrite and hydrochloric acid at 0-5\textdegree{}C. The diazotised drug is treated with ammonia solution to form yellow colour solution, which was measured at 425 nm.

(c). Dapsone:

Various techniques adopted for the estimation of Dapsone are Spectrophotometric method\textsuperscript{23-34}, Colorimetric method\textsuperscript{35},

Iskender etal\textsuperscript{23}, have developed a method for the determination of dapsone in tablets by spectrophotometrically using 1, 2-Naphthoquinone-4-
sulfonic acid sodium salt. The method was based on the chromophore formation after reaction with sodium 1,2-naphthoquinone-4-sulfonate (NQ). The reaction proceeded quantitatively at pH 2 and 60° within 30 minutes when the molar ratio of the reagent to dapsone was 10. After completion of the reaction, the derivative formed; dapsone-NQ, was extracted from the aqueous solution with chloroform/butyl alcohol (3:1). dapsone-NQ, showed maximum absorbance at 440 nm.

Zarapker et al.24, proposed a simple spectrophotometric method for the estimation of dapsone from pharmaceutical preparation. The method based on coupling of the diazotized dapsone with 8-anilino-1-naphthalene sulfonic acid, resorcinol or ß-naphthol in alkali medium and measurement of absorbance at 550, 440 or 490 nm respectively.

Shoukrallah et al.25, determined dapsone by spectrophotometric method using 9-chloroacridine as a chromomeric reagent. The method was based on condensation reaction of 9-chloro acridine and the amino groups of dapsone. The reaction variables were investigated and optimized. The resultant coloured product was measured at 443 nm.

El-Dolkiny et al.26, have developed two methods for the micro determination of dapsone in bulk and dosage forms by spectrophotometric method. In the first method, sodium 1, 2- naphthoquinone-4-sulfonate was
used as a reagent for the colorimetric determination of the drug. The second
method used coupling of the diazotized primary aromatic amino groups in
dapsone with barbituric acid.

Rao B.C etal\textsuperscript{27}, proposed a simple and sensitive spectrophotometric
method for the estimation of dapsone. The method was based on schiff's
base formation with 4-dimethyl amino cinnamaldehyde in the presence of
methanolic sulfuric acid. The red coloured chromogen had absorption
maxima at 540 nm.

Rami Reddy etal\textsuperscript{28}, proposed a new spectrophotometric method for the
estimation of dapsone. The method was based on the bromination of
dapsone with brominating mixture. The excess brominating mixture was
reacted with potassium iodide to produced yellow colour. The absorbance of
yellow colour solution is measured at 350 nm.

Rami Reddy etal\textsuperscript{29}, developed a simple spectrophotometric method for
estimation of dapsone form pharmaceutical preparations. The method is
based on the diazotization of dapsone followed by the addition of ammonia
solution. The yellow colour developed was measured at 445 nm.

Toral, M.I etal\textsuperscript{30}, proposed a simple and fast spectrophotometric
method for the simultaneous determination of dapsone and pyrimethamine
by first-order digital derivative spectrophotometry. Acetonitrile was used as
a solvent to extract the drugs from the pharmaceutical formulations, and the samples were subsequently evaluated directly by digital derivative spectrophotometry. The simultaneous determination of both drugs was performed by the zero-crossing method at 249.4 and 231.4 nm for dapsone and pyrimethamine, respectively. The best signal-to-noise ratio was obtained when the first derivative of the spectrum was used. The excipients of commercial pharmaceutical formulations did not interfere in the analysis. Chemical and spectral variables were optimized for determination of both analytes. A good level of repeatability, 0.6 and 1.7% for dapsone and pyrimethamine, respectively, was observed. The proposed method was applied for the simultaneous determination of both drugs in pharmaceutical formulations.

Nagaraja, P et al., proposed a rapid, simple and sensitive spectrophotometric method for the determination of some sulfa drugs. The method is based on the formation of orange yellow colored azo product by the diazotization of sulfonamides, viz., dapsone (DAP), sulfathiazole (SFT), sulfadiazine (SFD), sulfacetamide (SFA), sulfamethoxazole (SFMx), sulfamerazine (SFMr), sulfaguanidine (SFG) and sulfadimidine (SFDd) followed by a coupling reaction with 3-aminophenol in aqueous medium. Absorbance of the resulting orange yellow product is measured at 460 nm.
and is stable for 6 days at 27 degrees C. Beer's law is obeyed in the concentration range of 0.05-8.0 μg/ml at the wavelength of maximum absorption. The method is successfully employed for the determination of sulfonamides in various pharmaceutical preparations and common excipients used as additives in pharmaceuticals do not interfere in the proposed method.

Wang H.Yetal\textsuperscript{32}, have developed Spectrophotometric method for determination of dapsone. The dapsone reacts with sodium 1, 2-naphthoquinone-4-sulfonic in pH 6.98 buffer solution to form a salmon pink compound, and its maximum absorption wavelength is at 525 nm, \( \epsilon_{525} = 3.68 \times 10^4 \text{ mol}^{-1} \text{ cm}^{-1} \). The absorbance of dapsone from 0.40 -10 μg/ml obeys Beer's law. The linear regression equation of the calibration graph is \( C = 0.2334 \ A + 0.01288 \), with a linear regression correlation coefficient of 0.9998, the detection limit is 0.24 μg/ml and recovery is from 99.2 to 102.4%. Effects of pH, surfactant, organic solvents, foreign ions, and standing time on the determination of dapsone have been examined. This method is simple and can be used for the determination of dapsone in injection solution of dapsone. The results obtained by this method agreed with those by the official method.
Revanasiddappa, H.D and Manju, B\textsuperscript{33}, have determined metoclopramide, dapsone, p-aminobenzoic acid, and cisapride in both pure and dosage forms by spectrophotometric method. The method is based on the diazo-coupling reaction of metoclopramide, dapsone, p-aminobenzoic acid, and cisapride with a new coupling agent, acetyl acetone, in an alkaline medium. The optimum reaction conditions and other analytical parameters are evaluated. The influence of the substrates commonly employed as excipients with these chemotherapeutic agents has been studied.

Omran, A.A\textsuperscript{34}, proposed a rapid, sensitive and selective spectrophotometric method for the quantitative determination of dapsone (DAP) and metoclopramide hydrochloride (MCP) in both pure and dosage forms. Individual and simultaneous methods are based on the diazo coupling reaction of these drugs with benzoylacetone (BAC) in alkaline medium. The resulting azo dyes exhibit maximum absorption at 437 and 411 nm with a molar absorptivity of $4.14 \times 10^4$ and $2.97 \times 10^4$ mol\textsuperscript{-1} cm\textsuperscript{-1} for DAP and MCP, respectively. Simultaneous determination of DAP and MCP was developed utilizing first-order digital derivative spectrophotometry. All variables have been optimized. No interferences were observed from drug excipients and the validity of the methods was tested against reference methods.
Shetty et al\textsuperscript{35}, have developed a specific colorimetric assay for dapsone in biological fluids. The original Bratton and Marshall method for sulfanilamide assay was modified for differential assay of dapsone (DDS) even in the presence of other diazotizable compounds. The property of the dapsone diazo derivative to precipitate out upon into coupling with N- (1-naphthyl) ethylene diamine was used to differentiate this sulfone from that of other diazotizable compounds.

\textbf{(D) Paracetamol:}

The various techniques adopted for the estimation of paracetamol are Spectrophotometric method\textsuperscript{36-54}, H.P.L.C method\textsuperscript{55-59}, Spectrofluorimetric method\textsuperscript{60}, Electro chemical\textsuperscript{61}, Rapid Liquid Chromatographic detection\textsuperscript{62}, Polarographic method\textsuperscript{63}

Menon et al\textsuperscript{36}, proposed a method for the analysis of paracetamol in drugs samples by measuring the absorbance at 248 nm. in methanol. The method has been applied to paracetamol tablets. Prasad and Durga\textsuperscript{37}, have determined paracetamol in solid dosage form by using oxidation reagent potassium ferricyanide in the presence of 1N sodium hydroxide and measurement of the absorbance of the oxidized product at 480 nm.
Chowdary and Rao\textsuperscript{38}, determined paracetamol by reacting the hydrolysed product of paracetamol with potassium dichromate to form a stable violet coloured chromogen and measuring the absorbance at 500 nm.

Erk et al\textsuperscript{39}, developed a method for the determination of paracetamol and hyoscine-n-butyl bromide in film-coated tablets by precipitating hyoscine-n-butyl bromide with ammonium reineckate at pH 6.0 and reading the absorbance of the solution of the precipitate in acetone at 520 nm. Orbery et al\textsuperscript{40}, proposed a simple method for the estimation of paracetamol and aspirin in dosage forms by using second order derivative spectroscopy method.

Gangwal et al\textsuperscript{41}, determined paracetamol and mefenamic acid in their combined dosage forms by using simultaneous spectrophotometric method based on the native UV absorbance maxima of mefenamic acid and paracetamol in 0.02 M sodium hydroxide. Mefenamic acid has two absorption maxima, at 285 nm and 333 nm., paracetamol has absorption maximum at 257 nm.

Anwar et al\textsuperscript{42}, proposed a simple and rapid spectrophotometric method for the determination of aspirin and paracetamol in pharmaceuticals. This method was based on the oxidation of aspirin or paracetamol with iron (III) ions. The resulting iron (II) formed a coloured complex with 1,10-
phenanthroline. The absorbance of this iron complex was measured at 510 nm.

Ravisankar et al.\textsuperscript{43}, developed for simultaneous determinations of paracetamol and chlormezanone in combined tablets formulations. The maximum absorbance of paracetamol measured at 243.6 nm and chlormezanone measured at 228 nm.

Mashru et al.\textsuperscript{44} proposed a simple and sensitive UV spectrophotometric method for simultaneous determination of chlorzoxazone and paracetamol based on absorption ratio technique. Bogachyk et al.\textsuperscript{45}, proposed a simple UV spectrophotometric method for determination of paracetamol and mefenamic acid in tablets formulations.

Nagaraja et al.\textsuperscript{46}, proposed a rapid, sensitive and simple spectrophotometric method for the determination of paracetamol and phenacetin by using sodium 1,2 naphthoquinone-4-sulfonate and acetyltrimethyl ammonium bromide in alkali medium. The absorbance was measured at 570 nm and 500 nm.

Rami Reddy and Chakravarthy\textsuperscript{47}, proposed a new spectrophotometric method for determination of Paracetamol in pharmaceutical preparations. This method is based on the bromination of the Paracetamol with brominating mixture. After bromination the excess brominating mixture is
treated with KI. The yellow colour developed was measured at 350nm against distilled water as blank.

Usifoh et al., developed a method for the determination of Paracetamol in raw material and in pharmaceutical dosage form. The method is based on measuring the intensity of the yellow colour developed when acetaminophen is allowed to react with p-dimethyl amino benzaldehyde in 2M HCl after heating. The colour absorbs in the visible region of 450 nm.

Amin and Alaa, have developed a spectrophotometric method for the estimation of Paracetamol. The method is based on its reaction with Pyrocatechol violet under basic conditions to form ion-pair complex. The absorption max. of the coloured ion-pair complex formed is observed at 652nm. Beer's law is obeyed over the concentration range 0.5-34 mg/ml.

Nameh et al. proposed a sensitive method for the determination of paracetamol in pharmaceutical preparations. The reaction of paracetamol with per sulfate was carried out in alkali medium at 40°c, for 10 minutes then determined at 315 nm.

Toral et al., developed a method for the determination of mefenamic acid and paracetamol in pharmaceutical formulations by using a direct and simple first derivative spectrophotometric method.
Ozgur et al\textsuperscript{52}, estimated paracetamol and dipyrone in combined dosage form using derivative spectrophotometric method using 'zero crossing' technique of measurement at 229.2 nm and 217.9 nm for paracetamol and dipyrone.

Bhatia et al\textsuperscript{53}, developed economical procedure for simultaneous estimation of diclofenac sodium chlorzoxazone and paracetamol in three component tablet formulations. This method employ first derivative UV spectrophotometry and simultaneous equations for the simultaneous estimation of the three drugs by using 0.02M sodium hydroxide, diclofenac sodium has an absorbance maxima at 276 nm, chlorzoxazone has an maximas at 244 nm and 288 nm and paracetamol has an absorbance maxima at 257 nm.

Bhatia et al\textsuperscript{54}, developed a simple procedures for simultaneous determination of paracetamol and chlorzoxazone in two component tablet formulations. This method employed first-derivative, UV spectrophotometry and simultaneous equation for the determinations of the two component drugs by using 0.02M sodium hydroxide, chlorzoxazone showed two absorption maxima at 244 and 288 nm, and paracetamol had an absorption maxima at 257 nm.
(e). Salbutamol:

The literature survey reveals Spectrophotometric method\textsuperscript{64-70}, Colorimetric method\textsuperscript{71,71}, Voltammetric study\textsuperscript{73}, HPLC method\textsuperscript{74}, Fluorimetric method\textsuperscript{75}, Liquid Chromatographic method\textsuperscript{76}, HPLC with Electrochemical detection\textsuperscript{77}, methods for determination of salbutamol and its formulations.

Bakry et al\textsuperscript{64}, proposed a method for determination of salbutamol sulfate by using chlorinated quinones in the presence or absence of acetaldehyde. Halogenated quinones were used to form coloured charge-transfer complexes with salbutamol base.

Parimoo et al\textsuperscript{65}, developed a method for the simultaneous determination of salbutamol and bromhexine hydrochloride in tablet preparations by difference spectrophotometric method. This method comprised the measurement of the absorbance of a solution of the drug mixture in pH 2.0 buffer solution relative to that of an equimolar solution in 0.1N methanolic sodium hydroxide at wavelengths of 310 and 280 nm.

Reddy et al\textsuperscript{66}, proposed a simple and sensitive visible spectrophotometric method for the determination of salbutamol and terbutaline in bulk samples and pharmaceutical preparations. The method
was based on the formation of the coloured species with 2,2'-Bipyridine and ferric chloride.

Chowdary and Rao\textsuperscript{67}, have developed a method for the determination of salbutamol and terbutaline in bulk and in pharmaceutical sample by using simple and sensitive visible spectrophotometry. This method was based on their oxidation with ferric chloride and subsequent complexation of Fe (II) formed with 2,2-bipyridyl to form a red complex with a \( \lambda \) max at 520 nm.

Singhvi and Chaturvedi\textsuperscript{68}, have developed three simple, accurate, economical and reproducible spectrophotometric methods for simultaneous determination of salbutamol and theophillin in combined dosage form in tablets. The first method employed the solving of simultaneous equation by using 244.6 and 274.6 nm as two wavelengths. The second method involved second derivative UV spectroscopy. The two wavelengths selected for this method were 314.0 and 283.2 nm. The third method was based on the two wavelength calculations.

Rathore et al\textsuperscript{69}, have developed a method for the determination of salbutamol and bromhexine in tablets by using simple spectrophotometric method.

Bhatt et al\textsuperscript{70}, have determined salbutamol sulphate and its dosage forms. Salbutamol sulfate on treatment with sodium hydroxide, sodium periodate
and acetyl acetone produced a yellow coloured chromogen with maximum absorbance at 412 nm.

Guha et al\textsuperscript{71}, developed colorimetric method for the determination of salbutamol. The method was based on the treatment of the drug with ferric chloride solution. A light violet solution was developed and its intensity was measured at 440nm.

Viswanath et al\textsuperscript{72}, determined salbutamol in pharmaceutical samples by reaction with diazotized phenyl hydrazine 4-sulphonic acid sodium salt and measurement of the absorbance of the product at 440 nm.

(f). Ranitidine:

The literature survey reveals Spectrophotometric method\textsuperscript{78-81}, HPLC method\textsuperscript{82-84}, Liquid Chromatographic method\textsuperscript{76}, methods for determination of ranitidine and its formulations

Hassan, E.M and Belal, F\textsuperscript{78}, have developed four new methods using titrimetry and spectrophotometry for the determination of ranitidine hydrochloride (RNH) with potassium bromate as the oxidimetric reagent and acid dyes, methyl orange, indigo carmine and metanil yellow. In direct titrimetry (method A), the drug is titrated directly with bromate in acid medium and in the presence of excess of bromide using methyl orange indicator. In back titrimetry (method B), the drug is treated with a measured
excess of bromate in the presence of bromide and acid, and the unreacted bromine is determined iodometrically. Both spectrophotometric methods are based on the oxidation of RNH by a known excess of bromate in acid medium and in the presence of excess of bromide followed by estimation of surplus oxidant by reacting with either indigo carmine (method C) or metanil yellow (method D), and measuring the absorbance at 610 or 530 nm. In methods B, C and D, reacted oxidant corresponds to the drug content. The experimental conditions are optimized. Titrimetric procedures are applicable over the ranges 1-10 mg (A) and 1-17 mg (B), and the reaction stoichiometry is found to be 1:1 (BrO(-)(3): RNH). In spectrophotometric methods, the absorbance is found to increase linearly with increasing concentration of RNH, which is corroborated by the calculated correlation coefficient (r) of 0.9984 (C) and 0.9976 (D). The systems obey Beer's law for 2-12 and 1-7 microg ml(-1), for methods C and D, respectively. Method D with a molar absorptivity of 9.82 x 10(4) l mol(-1) cm(-1) is found to be more sensitive than method C ( epsilon = 2.06 x 10(4) l mol(-1) cm(-1)). The limits of detection and quantification are reported for both the spectrophotometric methods. The proposed methods were applied successfully to the determination of RNH in tablets and injections. The
reliability of the assay was established by parallel determination by the official method and by recovery studies.

Perez-Ruiz T et al\textsuperscript{79}, proposed a simple spectrophotometric method for determination of trace amounts of ranitidine using bromothymol blue with a flow system. The determination of ranitidine in the range of $1 \times 10^{-5} - 1 \times 10^{-4}$ mol l\(^{-1}\) was possible with a sampling frequency of 40 samples h\(^{-1}\). The method was satisfactorily applied to the determination of ranitidine in pharmaceutical preparations and the recovery was quantitative and no interference.

Apostu, M, et al\textsuperscript{80}, proposed a new visible spectrophotometric assessment by using the reaction between ranitidine and eosine. We carried out our determinations at 505 nm, where the absorbency of ranitidine-eosine complex is maxima, and we have established the optimal reaction conditions.

Walash, M,I et al\textsuperscript{81}, have developed an accurate and simple kinetic method for the determination of ranitidine and nizatidine in pure form and in pharmaceuticals. The method is based on the reaction of the compounds with 7-chloro-4-nitrobenz-2-oxa-1,3-diazole in pH 7.4 borate buffer at 60 degrees C for a fixed time of 25 min for both compounds. The absorbance of the reaction product is measured at 495 nm for ranitidine and nizatidine.
Calibration graphs were linear over the concentration range of 2-20 microg/mL, with limits of detection of 0.13 (3.7 x 10^{-7} M) and 0.25 microg/mL (7.5 x 10^{-7} M) for ranitidine and nizatidine, respectively. The proposed method was applied successfully to the determination of ranitidine in tablets and ampoules with average recoveries of 100.26 +/- 0.69 and 100.29 +/- 0.59\%, respectively, and to the determination of nizatidine in capsules with an average recovery of 104.26 +/- 0.44\%. The results obtained are in good agreement with those obtained by the other methods used for comparison. A proposal of the reaction pathway is also presented. (f). Cetirizine:

The literature survey reveals Spectrophotometric method^{85}, HPLC method^{86-87}, Liquid Chromatographic method^{88}, methods for determination of cetirizine and its formulations

Drozd, J., et al^{85}, proposed a spectrophotometric method for the determination of cetirizine dihydrochloride in pharmaceuticals by first-, second-, third- and fourth- order derivative spectrophotometry by using "peak-peak" (P-P), and "peak-zero" (P-0) measurements. The calibration curves are linear within the concentration range of 7.5-22.5 microg ml^{-1} for cetirizine dihydrochloride. The procedure is simple, rapid and the results are reliable.
(b). Objectives of the present investigation

Drugs and pharmaceuticals play a very significant role in the present days for the reason that these drugs find important application in the 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 manufactures. 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 the spurious and substandard drugs into market, which definitely will have an adverse effect on the human beings at large.

It is with this challenge in mind, the author has taken up his thorough investigations to know and 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 has been paid to such
simple and rapid spectrophotometric methods for the assay of drugs is available in literature. Several instrumental techniques (HPLC, GC, Fluorimetry, NMR, IR, UV and Visible regions) are available for the assay of drugs. These methods are either expensive or do not give reproducible results are found reported in literature. Usually spectrophotometric technique is simple and less expensive. The selectivity and sensitivity of the spectrophotometric methods depends only on the nature of chemical reactions involved in colour development and not on the sophistications of the experiment.

UV and Visible spectrophotometric methods are highly versatile, sensitive and reproducible. In an attempt to develop new UV and Visible spectrophotometric techniques for the evaluation of purity of the pharmaceutical preparations.