CHAPITRE - 2

LITERATURE REVIEW

2.1 PAST WORK DONE ON ALFUZOSIN EXTENDED RELEASE FORMULATION

Sritharan et al.\textsuperscript{33} to evaluate the in vivo and in vitro performance of conventional monolithic matrix tablet compared to three layer tablet. Alfuzosin hydrochloride extended release tablets to be taken once daily were formulated with 10 mg Alfuzosin hydrochloride. The release was extended by using swellable polymers like polyethylene oxide and Hydroxypropylmethyl cellulose.

Monzurul Amin Roni et al.\textsuperscript{34} Alfuzosin hydrochloride extended release tablets were formulated as single matrix tablet with hydrophilic (HPMC) and hydrophobic (Ethyl cellulose) polymers. Dissolution data optimized formula was fitted into zero, first order, & Higuchi’s release kinetics. Korsmeyer’s equation explained that the drug release was followed both diffusion and erosion mechanism in all cases.

Madhu E Nicholas et al.\textsuperscript{35} Alfuzosin hydrochloride extended release matrix tablets were manufactured by wet granulation method by using hydrophilic polymers (HPMC K100M) and hydrophobic polymers (hydrogenated castor oil and ethyl cellulose). The matrix granules were manufactures by mixing the drug with hydrogenated castor oil using binder solution contains ethyl cellulose in different amounts. The dried granules were compressed with HPMC K100M at optimized concentration of ethyl cellulose. The optimized batch’s drug
release follows zero order kinetics by anomalous (non-fickian) diffusion.

Quan Liu et al.\textsuperscript{36} Gastro-retentive matrix tablets of Alfuzosin hydrochloride 10 mg designed, characterized and fitted in to zero-order kinetics. Triple layer and bi-layer composite matrices contains Polyethylene oxide, Hydroxylpropylmethyl cellulose, Sodium bicarbonate, Citric acid and Polyvinyl pyrrolidone. The drug release principle follows swelling and erosion.

Anroop et al.\textsuperscript{37} Alfuzosin hydrochloride controlled-release matrix tablets formulated by direct compression technique using low viscous hydroxylpropylmethyl cellulose (HPMC K-100 and HPMC 15cps). The release rate was not highly significant with different ratios of HPMC K-100 and HPMC15cps.

Utpal Kumar Sanki \textit{et al.}\textsuperscript{38} Hot-melt granulation techniques used for development of Alfuzosin modified release Tablets using mono glycerides and di-glycerides as rate controlling membranes. The optimized formulation was bioequivalent with respect to rate and extends of absorption to the reference formulation.

\textbf{2.2 PAST WORK DONE ON ALFUZOSIN ANALYTICAL METHODS}

Akhilesh Chandra \textit{et al.}\textsuperscript{39} Simple and sensitive visible spectrophotometric methods were develop to estimate the Alfuzosin hydrochloride with spectroscopic methods (I and II). Method I obeyed Beer’s law in the concentration range of 2-8 µg/mL with maximum absorption at 783 nm. Method II chromogen also obeyed Beer’s law in the concentration range of 10-50 µg/mL with maximum absorption at
510 nm. The both methods were validated statistically agreement with the labeled amounts.

Adsule Prajakta V et al.\textsuperscript{40} was developed a simple, economical, precise and accurate three UV spectrophotometric method for the determination of Alfuzosin in bulk and formulations. In method A, method B & method C maximum absorbance measured at 244.99 nm, 243.34 – 246.63 nm (AUC) & 235.12 nm (First order derivative). Linearity was observed in the concentration range of 2.5 - 30µg/mL.

Safwan Ashour et al.\textsuperscript{41} was developed a simple, sensitive and fast spectrophotometric method for the estimation of Alfuzosin hydrochloride in pure form and formulation dosage form by using indicators like bromothymol blue, bromocresol purple, bromophenol blue absorbance measured at 412nm, 407nm and 413nm respectively. The percentage of recovery was 98.80 – 101.33 %.

M.Vamsi Krishna et al.\textsuperscript{42} was developed a simple, accurate and precise three spectrophotometric methods for estimation of Alfuzosin hydrochloride in drug substance and tablet formulation. The first method was developed based on reaction between Alfuzosin and ninhydrin in N, N-dimethylformamide medium to produce a colour and measuring the absorbance at 575nm. The second method was developed based on reaction between Alfuzosin with ascorbic acid in to produce colored product which measures absorbance at 530nm. The third method was developed based on reaction of Alfuzosin with p-benzoquinone to form a colored product which measures at 400 nm. All three procedures are validated.
Dipti B Patel et al. was developed both RP-HPLC and HPTLC for the estimation of Alfuzosin hydrochloride in drug substance and in pharmaceutical formulation. In HPLC method the separation was done by using C18 250×4.6 mm, 5μm, water:methanol:acetonitrile (60:30:10 v/v) as the mobile phase, flow rate 1.0mL/min and detection at 245nm. In HPTLC method the separation was by using an aluminium-backed layer of silica gel60F254, toluene:methanol:triethylamine (3:1:0.2 v/v), detection at 245 nm over the range of concentration 50-400ng/spot.

K.S Bharath kumar et al. a simple rapid and precise reverse phase high pressure liquid chromatography method was developed and the same validated for the determination of Alfuzosin hydrochloride in tablet dosage form. Parameters of method are the flow rate at 1 mL/min, Retention time and injection volume set at 10min and 10μL with U.V detection at 245nm. And the percentage of recovery found to be 98.8 percentage.

Mani Ganesh et al. an isocratic reversed phase high-performance liquid chromatographic method with ultraviolet detection at 245 nm has been developed for the determination of Alfuzosin hydrochloride in pharmaceutical dosage form. Separation of Alfuzosin developed by using a column InertsilODS-3V (15 cm x 0.46 cm, 5μm) at ambient temperature (25 ± 2°C) using Acetonitrile:Water: Tetrahydrofuran: Perchloricacid (250:740:10:1) as mobile phase with flow rate of 1mL/min. The developed method was validated for its selectivity, accuracy, precision and linearity. This method was found
Vandana P. Patil et al,\textsuperscript{46} A reverse phase high performance liquid chromatographic method has been developed for the estimation of Alfuzosin hydrochloride in the pharmaceutical formulation using RP-C18 column, Tetrahy-drofuran, Acetonitrile and buffer pH 3.50 (1:20:80 ) as a mobile phase with flow rate of 1.5 mL/min and scanned at 254.0 nm. The method was validated and RSD was found to be less than 2% it reveals that method is accurate.

2.3 PAST WORK DONE ON ALFUZOSIN BIO ANALYTICAL METHODS

Utpal Kumar Sanki et al.\textsuperscript{47} The study was to evaluate in vitro-in vivo performance of Alfuzosin modified release tablet in healthy human subjects. The in vivo pharmacokinetic parameters under fasting conditions between test and reference formulations (Uroxatral 10mg extended release tablets) were comparable. The 90% CI, geometric mean ratio (%) and power of Cmax, AUC0-T, and AUC0-Inf of the fasting study for the test and reference formulation were performed. The developed formulation was safe to use since there were no any adverse events occurred while conduction of the clinical trial on the healthy subjects.

Madhura V. Dhoka et al.\textsuperscript{48} Rapid, precise, accurate, simple, selective, and sensitive high pressure liquid chromatography method (HPLC) and high pressure thin layer chromatography method (HPTLC) methods for the determination of Alfuzosin in human plasma have
been developed. HPLC method was developed by using HiQ sil C8 HS column, mobile phase containing mixture of Acetonitrile: Sodium acetate buffer with n-hexane sulphonic acid salt having pH 4.0, at the flow rate of 1mL/min and detection was performed at 244nm. The HPTLC separation was developed on the Aluminium plates coated with silica gel 60 F254 using Toluene: Methanol: Triethylamine as mobile phase and found at 244nm with TLC Scanner.

### 2.4 Past Work Done on Citicoline Formulation

Note: Very less work has been done on citicoline controlled release drug delivery systems.

Katarzyna Swiader et al.\(^49\) the formulation and evaluation of citicoline enteric coated tablets by using wet granulation method. Aqueous dispersion enteric coats showed good physical resistance in hydrochloric acid of pH 1.2 with no drug release for two hours. The coated tablets dissolved rapidly when tablets were removed from acid medium and dropped in the pH 6.8 phosphate buffer.

Amol R. Jipkate et al.,\(^50\) Citicoline Sustained Release Tablets were prepared by using hydroxypropylmethyl cellulose (HPMC) at different concentrations of matrix system by wet granulation method. Hydroxylpropylmethyl Cellulose proved as a rate controlling polymer by the diffusion-dissolution controlled mechanism.

### 2.5 Past Work Done on Citicoline Analytical Methods

Neetu Sachan et al.,\(^51\) simple, accurate, precise, rapid and low cost method developed for the determination of Citicoline by using double beam UV spectrophotometer, it obeyed Beer Lambert’s law at the
concentration range of 5-50μg/mL and maximum absorption at 272 nm. Method was successfully validated in order to verify selectivity, accuracy, linearity and precision.

Sagar Suman Panda et al. was developed a novel, precise and accurate method for the estimation of citicoline sodium in tablet dosage form by difference spectrophotometric method. Citicoline sodium shows two different forms that shows different absorption spectra in acidic (0.1M HCL) & basic (0.1M NaOH) medium. The maxima and minima in the difference spectra of citicoline sodium were found to be 239nm and 283nm respectively. Linearity in the range of 1-50μg/mL. The percentage recovery from the tablet dosage form was 98.47%.

Malipatil S.M et al. was developed simple, accurate, precise and sensitive two spectrophotometric methods in UV and visible region for the estimation of citicoline in pharmaceutical dosage form. The method A shows maximum absorption at 272 nm in distilled water. The method B was developed the reaction of 3-methyl-2-benzothiazolin-2-one hydrazone with citicoline sodium in presence of ferric chloride solution to produce a yellow orange product. The maximum absorption shows at 625 nm. Both the methods were obeyed Beer’s law in the concentration range of 10-70 μg/mL and 50-250 μg/mL respectively.

G.Raveendra babu et al. was validated specific and stability indicating method was developed for estimation of citicoline and its related substances in oral drops formulation on reversed-phase liquid chromatographic method. Detection was performed at 280 nm and the
validation data showed that method is specific, sensitive and reproducible for assay and related substances.

Sonali O. Uttarwar et al. Method was developed for estimation of citicoline on reverse phase liquid chromatography in citicoline sustained release tablets. Separation was achieved by using column hypersil BDS C18250×4.6 mm, 5µ particle size, buffer: methanol (98:2 v/v), flow rate 1.0 mL/min, injection volume was 20 µl and detection at 280 nm. Developed method was validated for precision, accuracy, specificity, linearity, Robustness, Ruggedness and solution stability.

K.Tulasi et al. analytical method was developed for the estimation of citicoline from dosage form by using isocratic reverse phase high performance liquid chromatography method, ammonium acetate and methanol used as a mobile phase, Colum C18, 250mm×4.6mm, 5µm, run time 10 min, flow rate 0.8 mL/min, injection volume 20 µL detection at 270nm. Linearity was observed in the range of 0.2 – 200 µg/mL. The RSD for precision was found to be less than 2.0 %.

Raveendra B.Ganduri et al. a stability indicating liquid chromatographic citicoline sodium assay method was developed from injection formulation. Citicoline was separated from the dosage form by using cosmosil C18 250×4.6 mm, 5µm, phosphate buffer and methanol (95.0:5.0%v/v), flow rate 1.0 mL/min, injection volume 20µL, runtime 25 min and detection wavelength 276nm. The accuracy and precision of the method was found to be 98.30 % and RSD less than 1.0 % respectively.
Sanjay Surani et al.\textsuperscript{58} a accurate, simple, specific, and precise spectrophotometric method for the estimation of citicoline sodium in drug substance and tablets. Solvent used were 0.1N Sodium hydroxide and double distilled water, with a absorption maxima of 272 nm. A linear relationship in the range of 5 to 55 $\mu$g/mL with a correlation coefficient was found 0.998.

2.6 PAST WORK DONE ON CITICOLINE TABLETS BIOANALYTICAL METHODS

Keguang Chen et al.\textsuperscript{59} Developed and validated a simple, rapid HPLC Method for the determination of uridine (i.e. a Metabolite of citicoline) in human plasma. Uridine was extracted from plasma by simple precipitation Method, amoxicillin used as internal standard. Uridine separation was carryout by using C18 100×4.6mm,2.6µ column, mobile phase of 0.05 M phosphate buffer adjusted pH to 3.5 – methanol (98:2 v/v)and flow rate 0.8mL/min. The standard calibration curve of uridine was linear over a concentration range of 0.02 – 2.0 $\mu$g/ mL. The relative bioavailability of citicoline sodium tablets was 92.7%.The citicoline tablet and capsules are bioequivalence.

Amlan Kanti Sarkar et al.\textsuperscript{60} was developed and validated a simple, rapid high performance liquid chromatography – tandem mass spectrometry method for the determination and pharmacokinetic investigation of choline (active metabolite of Citicoline).Metformin used as a internal standard, mobile phase of methanol – water (9 : 1 v/v),
the standard calibration curves were linear over the range of 0.05 - 5µg/mL.