2. Review of literature

From the Literature review it is unable to find the combined HPLC methods for their respective formulations of Temozolomide and Anastrozole are present in publications however, an analytical methods for individual analysis for Temozolomide and Anastrozole was published. It is felt necessary that to develop quantitative LC method for simultaneous determination of Temozolomide and Anastrozole for their respective formulations. It was also found that there are some analytical methods reported for the Temozolomide and Anastrozole separately and most of the works reported were done on the biological fluids.

With growing concerns over food safety and the need to increase sample-throughput in analytical testing laboratories, there is a constant requirement for accurate, simpler, faster and improved analytical methods. The complexity of food matrices and the presence of much potential interference, require specific and selective methods of analysis.

**Anastrozole** [16], [17], [18], [19], [20], [21], [22], [23], [24].

Kumar et al reported that Development and validation of spectrophotometric method for estimation of anastrozole bulk and pharmaceutical dosage formulation. Method was developed and validated by using a simple solvent system for anastrozole bulk and tablet dosage form. In the developed method, water and ethanol are used as solvents and $\lambda$-max was determined to be 221nm. The procedure was validated as per ICH rules for Accuracy, Precision, Detection limit, Linearity, Reproducibility and Quantitation limit. The linearity concentration range was 40-60µg/mL with the correlation coefficient of 0.9971. The percentage recovery for anastrozole was found to be 98.6 to 100.8%. Limit of detection and limit of quantitation values were found to be 1µg/mL and 3µg/mL. The method has been successfully used to analyze commercial solid dosage containing 1mg of anastrozole with good recoveries and proved to be robust. This provides shorter analysis time and conserves the solvent system. [5]

Srinivasulu et al reported that Reverse Phase HPLC method for analysis of Anastrozole in Pharmaceutical dosage forms. Simple and precise RP HPLC method was developed and validated for the determination of anastrozole in pharmaceutical dosage forms. Chromatography was carried out on an Inertsil ODS (250mmX 406 mm) C18 column using a mixture of Buffer:Acetonitrile (60:40) as The mobile phase at a flow rate 1.0 ml/min. The analyte was monitored using UV detector at 215 nm. The retention time of the drug is 6.431 min for anastrozole. The proposed method is found to be having linearity in the concentration range of 0.1 to 0.6 µg/ml with correlation coefficient of $r=0.9999$. The mean recoveries obtained for anastrozole are in the range 99.8-100.2%. The developed method has been Statistically validated and found simple and accurate. Due to its simplicity, rapidness, high precision and accuracy of the proposed method it may be used for determining anastrozole in bulk and dosage forms. [6]
Temozolomide. [21], [22], [23], [24], [28], [29], [30].

Saravanan et al reported that A Stability-Indicating LC Assay and Degradation Behavior of Temozolomide Drug Substances., This study deals with a stability indicating HPLC reverse phase method for quantitative determination of Temozolomide. A chromatographic separation was achieved on an Inertsil ODS 3V, 250 × 4.6 mm ID, 5 µm column using mobile phase A (buffer 5 mL glacial acetic acid in 1,000 mL of Milli Q water) and mobile phase B (methanol). Forced degradation studies were performed on bulk sample of Temozolomide using acid (0.5 N hydrochloric acid), base (0.5 N sodium hydroxide), oxidation (10% v/v hydrogen peroxide), heat (60 °C) and UV light (254 nm). Degradation of the drug substance was observed in base hydrolysis and oxidation. Degradation product formed under these conditions was found to be Imp-A. When the stress samples were assayed, the mass balance was close to 99.5%. The sample solution was stable up to 48 h at 5 °C and mobile phase was found to be stable up to 48 h at 25 °C. The developed method was validated with respect to linearity, accuracy, precision, robustness and forced degradation studies prove the stability indicating power of the method. [7]

Kunithala et al reported that, New, Simple, Precise, Rapid and Accurate Temozolomide RP-HPLC method has been developed and validated by using low cost materials to estimation of these Temozolomide in dosage forms. A new simple, precise, rapid and accurate, reproducible and selective reverse phase HPLC method has been developed for the estimation of Temozolomide in dosage form. It was resolved by using a mobile phase of Potassium dihydrogen phosphate: acetonitrile in the ratio 40:60 v/v at a flow rate of 1.0 ml/min. on HPLC system using UV -Visible detector at the wavelength of 287 nm. The column used was C18 (4.6 x 150mm, 5µm, Make: ODS) or equivalent .The linearity range was found to be 10-50 µg/ml. The proposed new method is found to be economic, sensitive, precise, rapid and reproducible. [8]

HPLC methods for simultaneous estimation. [25]

Bhosale et al reported that, RP-HPLC Method for Simultaneous Determination of Butenafine Hydrochloride and Betamethasone Dipropionate in a Cream Formulation. An RP-HPLC method has been developed for the simultaneous determination of butenafine hydrochloride and betamethasone dipropionate on a Inertsil C18 column (250cm4.6mmid) using a mobile phase gradient consisting of methanol and water at a flow rate of 1mL/min. Detection was carried out at 254nm.The method was validated with respect to specificity, linearity, accuracy, precision, ruggedness, and robustness. This method is simple, precise, and sensitive, and applicable for the simultaneous quantification of butenafine hydrochloride and betamethasone dipropionate in a cream formulation. [9]