2. Review of literature

2.1 General review

Now a days there is increase in the lifestyle related disease mainly cancer and cardiovascular diseases, therefore one finds it important to maintain quality of the life saving drugs like anti-cancer drugs. The validated analytical methods for genotoxic impurity in Imatinib Mesylate and Sorafinib tosylate revealed that there are very few analytical methods available for the determination of potential genotoxic impurity in bulk drug.

Selection of suitable analytical methods are based on the following

   Accuracy and Precision of the method
   a. Nature of the sample to be analyzed.
   b. Availability of the sample and concentration range which ensures sensitivity and range of concentration to be used for analysis.
   c. Interfering components.
   d. Physical and chemical properties of sample matrix.

Aims and Objective of the Proposed Research

✓ To develop selective methods which are simple reliable workable and economical under routine conditions.
✓ To evaluate and study the stability indicating nature of the method
✓ Validation of the analytical methods.
✓ To apply developed analytical methods to various formulations.

2.2 Literature review from pharmacopeias.

All country having their own regulatory body to control the quality of pharmaceutical drug substances and drug products.

From review of Indian pharmacopeias, United State Pharmacopeia, British pharmacopeia and European pharmacopeia, there is no analytical method is available for Imatinib mesylate and sorafinib tosylate.[15,16,17,18]
2.3 Literature review from Journal

Literature studies shows there are very few Reverse phase analytical methods has been developed and validated for Imatinib mesylate and sorafenib tosylate.

Analytical method for imatinib Mesylate is given below:

The HPLC method developed for the determination of Imatinib mesylate in capsule is accurate, precise, rapid and selective. It can therefore be easily and conveniently use for routine quality control analysis, particularly when large number of samples are encountered. The developed method was found to be specific, as there was no interference of the excipients which is confirmed by the absence of extra peaks\(^{(19)}\).

Quantitative HPLC method has been developed for Imatinib mesylate in rat serum. The method has demonstrated high sensitivity with lower limit of quantification of 25ng/ml and stability of imatinib mesylate in serum\(^{(20)}\).

A HPLC method with UV detection has been further developed, optimized and validated for the determination of imatinib concentration in mouse biological matrices (plasma, brain, spleen, kidney and liver). Optimization of the method also reveals the importance of pH accuracy in sample processing as well as in analytical conditions. The method is simple, quick and sensitive enough and has been successfully applied to assess imatinib accumulation in tissues after multiple oral dose administration to mice. Imatinib showed good tissue penetration except in brain where multiple dose administration did not produce any accumulation\(^{(21)}\).

The reversed-phase high-performance liquid chromatographic (RP-HPLC) method has been developed and validated for the simultaneous determination of imatinib mesylate and of the impurity product in Glivec capsules. The method was validated statistically
for its selectivity, linearity, precision, accuracy and robustness. Due to its speed and accuracy, the method may be used for quality control analyses\textsuperscript{(22)}.

An isocratic reversed-phase liquid chromatography method with UV detection has been developed for the purity evaluation of imatinib mesylate in bulk drug. The method was validated in terms of system precision, method precision, linearity, accuracy, limit of detection and limit of quantification\textsuperscript{(23)}.

Some reported analytical method for sorafenib tosylate is given below

Under the presently prescribed conditions, the recoveries of sorafenib were found to be 98.12 to 100.50\%. This indicates that commonly used excipients in pharmaceutical formulations were not interfering in the proposed method. This method is very useful for determination of sorafenib in pharmaceutical dosage forms. The observation of \% RSD less than 2.0 for both intra- and inter-day measurements also indicates high degree of precision. In the present method, we have established linearity range of 20-120 $\mu$g/mL; this linearity range covers all the strengths of sorafenib hence this method can be applied for quantifying the low levels of sorafenib in pharmaceutical dosage forms\textsuperscript{(24)}.

The electrochemical reduction behavior and determination of sorafenib was studied by differential pulse polarography at dropping mercury electrode. In this method the carbonyl group getting reduced to the saturated compound in a four electron processes and eduction mechanism has been proposed\textsuperscript{(25)}.

The method was used in routine practice to monitor plasma concentrations of sorafenib in cancer patients. Large interindividual variability and higher exposure in patients experiencing severe toxicity support the need for therapeutic drug monitoring to ensure an optimal exposure to sorafenib\textsuperscript{(26)}. 
The HPTLC method is for estimation of sorafenib tosylate and its formulation. The developed method is validated as per ICH guideline. The method can be used to determine the purity of drug available from various sources by detecting the related impurities\textsuperscript{(27)}.