

Chapter-2: Aims and objectives

2.1 AIMS

With the progression in new drugs developed in anticancer category, their impurities identification and structure elucidation is necessary. Hence, analytical method development for estimation of some anticancer drugs in presence of their degradation products were planned followed by forced degradation study to capture all possible degradation products, degradation kinetic study and impurity profiling study including detailed characterization of generated degradation products were planned.

2.2 OBJECTIVES

To achieve the above mentioned aims, following specific objectives for the study were planned to be followed for each of the selected drugs i.e. alectinib, nelarabine and gimeracil:

2.2.1 Analytical method development for estimation of anticancer drug in presence of their degradation products

- To develop the LC-UV-PDA method for estimation of selected anticancer drugs (alectinib, nelarabine, and gimeracil) in presence of their degradation products.
- As per ICH guideline, to validate the developed method to prove the efficiency of the analytical method.

2.2.2 Forced degradation study

- To conduct the forced degradation study as per ICH guideline in various stress conditions such as acid, alkali, oxidation, heat, UV and light.
- If required, to develop separate MS compatible analytical method for running the degraded samples in LC-MS or HRMS instruments.
- To identify the generated degradation products in UV, PDA or MS detector.

2.2.3 Degradation kinetic study

- If possible, to expose the drug in various conditions of temperature and time to understand the degradation kinetic behavior of drug.
- To identify the order of reaction for degradation of drug along with the estimation of some statistical results such as regress coefficient, rate constant and half life of the drug.

2.2.4 Isolation of major degradation products generated

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- To isolate the major degradation products using preparative HPLC for further detailed analysis on NMR and LC-MS for characterization

2.2.5 Characterization of all degradation products identified and/or isolated through preparative HPLC

- To characterize and identify the structure of unknown degradation products generated and observed through LC-UV-PDA or LC-MS detector.
- To run the degradation samples in HRMS/LC-MS instrument to have MS and MS/MS spectra so that fragmentation pattern of the degradation products can be understood.
- To run the degradation products isolated in NMR instrument to have NMR proton and carbon spectra which helps to understand the overall structure of the unknown compound by overall neighboring environment of the atoms (hydrogen and carbon) present in the structure.