PREFACE

Usually, the active pharmaceutical ingredients were manufacturing by a total synthetic process or by changes of natural processes, during the preparation of this development process, using the different type of solvents, reactive reagents, raw materials and intermediates. However, it was not easy to remove them totally from the synthetic process. So the presence of ppm level as impurities in APIs has become an increasing concern of various pharmaceutical companies, medical consultants, and regulatory authorities as it causes health risks in humans.

In genetics, **'genotoxicity'** describes the property of chemical agents that damages the genetic information within a cell causing mutations, which may lead to cancer. Evidence of genotoxicity includes genetic damage, cell death, and neoplastic transformation.

Any compound that produces a positive result in one or more assays as per the standard methods has historically been regarded as genotoxic, which may require further testing for risk assessment. These genotoxic impurities must be detected, identified and reported before clinical trial initiation to ensure patient safety and eventual drug approval. A threshold of toxicological concern (TTC) value of 1.5 μg/day intake of a genotoxic impurity is considered to be associated with an acceptable risk (excess cancer risk of <1 in 100,000 over a lifetime) for most pharmaceuticals.

A method capable of detecting the ppm level is an enormous challenge for the analyst and pharmaceutical companies to control these genotoxic impurities. Optimizing of a method for the quantification of genotoxic impurities at ppm level using ultraviolet-visible spectrophotometric, gas chromatography and high-performance liquid chromatography is a difficult task in the pharmaceutical industry as the sensitivity of these instruments is low. Hence the sensitivity of analytical technique must be increased for ppm levels quantification of impurities. This can be arrived by liquid chromatography (HPLC, UPLC, nano LC) coupled with mass spectrometry (MS).