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Impurity profiling for pharmaceutical development

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Abstract

Determination of potential impurities in drug substances (APIs) or drug products (DPs), including genotoxic and carcinogenic are critical issues relating evaluation of safety, stability, and Permitted Daily Exposure (PDE) values. Impurities could be introduced to the finished products during synthesis, purification, and storage of APIs, or in the mixing and pretreatment processes with the components of drug products. A protocol for the impurity profiling of pharmaceutical development was proposed and detailed in this report. The overall profiling scheme includes: (i) development and validation of an HPLC method for determination of API and DP, (ii) respective implement of the forced degradation and stress studies on API and DP, i.e. by subjecting samples to the acidic and alkaline hydrolysis, oxidation, heat, light, humidity and to the components of formulation, (iii) analysis of the degradants by HPLC, (iv) characterization of the molecular weights and collision activated dissociation (CAD) fragmentation pathways of API and DP by tandem mass spectrometric (MS/MS) Q1, precursor ion, product ion, and neutral loss scans, (v) structure elucidation, (vi) establishment of the API and DP degradation pathways and decomposition mechanisms, (vii) confirmation the chromatographic peaks by multiple-reaction monitoring (MRM), and (viii) determination of expiration duration data by formation kinetic study of impurities. Moreover, unique MS patterns and isotopic ratios contributed by stable isotopes in impurities, such as S-32/S-34, Cl-35/Cl-37, K-39/K-41, Cu-63/Cu-65, Br-79/Br-81, and ten stable isotopes of Sn-112 to Sn-124 etc can be also an essential tool for the elucidation of structure, mechanisms, and profiling.

Biography

Kung-Tien Liu has completed his Ph.D from National Taiwan University and worked in Institute of Nuclear Energy Research (INER) for the radiopharmaceuticals analytical methods R&D for more than 29 years. Since Oct. 2011, he is the R&D Division Manager of Pharmaceutical B. U., Everlight Chemical Industrial Corporation. He has published more than 20 papers in reputed journals, more than 10 patents and 2 book chapters relating pharmaceutical developments.