Abstract

The objective of the present investigation was to develop a stability indicating RP-HPLC methods for nelfinavir mesylate, linezolid, lacosamide and ritonavir drug substances as well as drug products. An another parallel objective was to separate, identify and characterize the major degradation products (DPs) of all the above drugs generated under hydrolytic, oxidative, photolytic and thermal stress conditions as advised in International Conference on Harmonization (ICH) guideline Q1A(R2). Nelfinavir mesylate and its tablet formulation was found to degrade under acidic, alkaline, oxidative and photolytic stress, while it was stable in neutral and thermal stress conditions. A total of three degradation products were formed, which were separated on a C-18 column employing a gradient HPLC method. Linezolid and its tablet formulation was found to degrade under acidic, alkaline, neutral and oxidative stress, while it was stable in photolytic and thermal stress conditions. A total of three degradation products were formed, which were separated on a C-18 column employing a gradient HPLC method. Lacosamide and its tablet formulation was found to degrade in acidic, alkaline and neutral stress and shown stable behavior against oxidative, photolytic and thermal stress conditions. A total of two degradation products were formed, which were separated on a C-18 column employing a gradient HPLC method. The two major degradation products of lacosamide were isolated by using column chromatography and a single dose acute toxicity study on both the degradation products was successfully performed. Among all the above drugs, ritonavir and its tablet formulation has shown highest labile behavior in acidic, alkaline and neutral stress while it was found to be stable to oxidative, photolytic and thermal stress conditions. A complete mass fragmentation pathway of all the drugs was first established with the help of multi-stage (MS^n) and MS/TOF accurate mass studies. Then stressed samples were subjected to LC–MS/TOF studies, which provided their fragmentation pattern and accurate masses. The mass spectral data were employed to characterize the DPs and assign structures to them. The total information was also used to establish the degradation pathway of all the drugs.