ABSTRACT

Chapter-1 is about general introduction of impurities and method development.

Chapter-2 describes about an unknown impurity formed in 50°C stability samples at 3 months in Lamivudine, Zidovudine and Nevirapine tablets for oral suspension which was detected by the new HPLC method. This degradation product was isolated by using preparative chromatography. The chemical structure of the degradant was elucidated by MS, ^1H-NMR, ^13C-NMR, DEPT and IR. The data indicated that the structure as 1-[5-Hydroxymethyl-4-(5-methyl-2,3-dihydro-[1,2,3]triazole-1yl]-tetrahydro-furan-2-yl]-5-methyl-1H-pyrimidine-2,4-(1H,3H)-dione. The mechanism of formation of this impurity is described in detail.

Chapter-3 is study about two potential unknown impurities with respect to Tenofovir disoproxil fumarate (TDF) in stability samples of 3M, 50°C were detected by HPLC method. These impurities were isolated and characterized using various spectral techniques. The structures of these two degradation products were characterized as [(1R)-2-[6-[[[1-[(2R,5S)-2-Hydroxy methyl]-1,3 oxathiolan-5-yl]-2-oxo pyrimidin 4yl] amino| methyl amino] purin 9-yl| 1 methyl- ethoxy] methyl (isopropoxy carbonyl oxymethoxy) phosphinic acid and 1-[2R,5S)-2-(Hydroxy methyl) 1,3 oxathiolan-5-yl]-4-[[1-[(2R,5S) -2-(Hydroxy methyl)-1'3-oxathiolan-5yl]-2-oxo-
The probable degradation pathway is discussed.

Chapter 4 is about development of a liquid chromatography method for separating the unknown impurities generated during the accelerated stability storage of Clopidogrel Bisulphate Tablets. Also, the newly developed method was used to identify the factors that contribute to the formation of these unknown impurities in the tablet formulation. All these studies were carried out by incubation of mixture of excipients and Clopidogrel API in 5:1 ratio at 80°C for 3 days. The new HPLC method was developed for separating the unknown impurities from the Clopidogrel Related Compound A. From the excipients compatibility data we hypothesized that these unknown impurities were generated due to the excipient Polyethylene Glycol that is present in the tablet both as a tablet lubricant as well as a part of the film coating system. Further these unknown impurities were characterized as Dihydro pyridinone Derivative, Decarbmethoxyalted Clopidogrel.

Chapter 5 describes a simple, sensitive and highly specific chromatographic method for the simultaneous determination of impurities of Lisinopril and Hydrochlorothiazide from their fixed dose combination. Symmetry C\textsubscript{18} column and a mobile phase comprising of 1-Hexane sulphonic acid sodium salt, Triethylamine, Orthophosphoric acid, Acetonitrile and Methanol has been used for this method. The developed method was validated as per ICH guidelines.
Chapter 6 describes the experiments carried out for identification and characterization of unknown impurity in Valsartan tablets. This impurity was detected at 6M 40°C/75% RH stability condition. This degradation product was characterized as N-[2'-(1H-Tetrazol-5-yl)-(1,1'-Biphenyl)-4-yl)methyl]-L-Valine. The probable mechanism for formation of this impurity is discussed.