Analytica Acta-2013

OMICS Group Conferences
Accelerating Scientific Discovery

4th International Conference and Exhibition on
Analytical & Bioanalytical Techniques

October 15-17, 2013 Las Vegas, NV, USA

Kinetic and pharmacokinetic analysis of treosulfan and its biologically active mono- and diepoxytransformers

Franciszek Glowka
Poznan University of Medical Sciences, Poland

Abstract

Treosulfan (TREO) is an alkylating agent, registered as Ovastat. Presently, TREO is applied as a promising meloablative agent with low organ toxicity. In physiological conditions it undergoes pH-dependent transformation into monoepoxy- (S,S-EBDM) and diepoxy- (S,S-DEB) transformers. Kinetics of the parent drug is generally known, but not its active transformers.

The aim of the study was assessment of kinetic and pharmacokinetic parameters of S,S-EBDM as well as SS-DEB and explanation of reasons of low concentrations of the transformers in patients receiving high doses of TREO as a part of conditioning regimen before hematopoietic stem cell transplantation (HSCT).

Method: Kinetics of TREO was investigated in phosphate buffers at pH 7.4 and temperature 37oC. The pharmacokinetics of TREO and its epoxides was studied in rabbits. The validated HPLC method with refractometric and UV detection was applied for determination of TREO, S,S-EBDM and S,S-DEB.

Summary: Transformation of TREO was the best described by kinetic model assuming two first order reactions: TREO S,S-EBDMS,S-DEB as well as first order reactions of hydrolityc decomposition of S,S-EBDM and S,S-DEB.

Formation parameters of S,S-EBDM (t0.5 1.5 h) and S,S-DEB (t0.5 3.3 h), and elimination of TREO (t0.5 1.6 h), S,S-EBDM (t0.5 0.069 h) and S,S-DEB (t0.5 0,046h) showed that after administration of TREO, both its active transformers demonstrate a formation-limited disposition. Then elimination of these epoxides proceeds at the same rate as TREO, but amounts of the transformers in the rabbits are much lower than TREO. It seems to explain the low levels of S,S-EBDM and S,S-DEB in plasma of patients after administration of TREO before HSCT.

Biography

Franciszek Glowka has completed his Ph.D. at Poznan University of Medical Sciences (PUMS) and postdoctoral traineeship from Division of Biomedical Sciences Imperial College London. He is professor and head of Department Physical Pharmacy and Pharmacokinetics, and Ass. Dean for Pharmacy Education, PharmD Program at PUMS. His fields of interests: bioanalysis of drugs, metabolites and endogenous steroids, stereoselective pharmacokinetics, therapeutic drug monitoring, pharmacogenetics and biopharmacy. He has published more than 50 papers in reputed international journals and over 80 contributed oral and poster presentations at national and international scientific meetings.