The dihydrouracil/uracil ratio in plasma, clinical and genetic analysis for screening of dihydropyrimidine dehydrogenase deficiency in colorectal cancer patients treated with 5-fluorouracil.

Abstract:
A rapid and cost-effective reversed phase high performance liquid chromatography (HPLC) method for quantification of dihydrouracil to uracil ratio (UH2/U) in plasma has been developed and used to screen for dihydropyrimidine dehydrogenase (DPD) deficiency in nine patients treated with 5-fluorouracil (5-FU). This HPLC method is based on the use of a simultaneous UV detection at 205 and 268nm during the analysis run of the plasma extract and taking into account the particularity that UH2 shows no absorbance response at 268nm. The plasma UH2/U ratio values evaluated by the use of our HPLC assay were found to be highly correlated with the plasma 5-FU-half-life values and were significantly associated with the toxic side effects, whereas, data set provided from genetic analysis of the coding sequences of the DPD gene (DPYD) were found to be insufficient to explain all the cases of the 5-FU-related toxicity pattern. The proposed HPLC assay could be available for routine clinical use for DPD deficiency assessment in patients prior to 5-FU administration.