Abstract:

The main aim of the current work is to investigate possible pharmacokinetic interactions between vardenafil hydrochloride (VAR), which is used for the treatment of erectile dysfunction and daclatasvir dihydrochloride (DAC), which is used for the treatment of chronic hepatitis C viral infection when they are concomitantly administered. Therefore, a sensitive and selective square-wave voltammetric method was developed and validated for simultaneous determination of VAR and DAC using disposable pencil graphite electrode (PGE) modified with xylenol orange (X.O.) flakes as an electrochemical sensor. A full investigation of the experimental parameters for obtaining the highest electroanalytical signal with sufficient resolution between the oxidation peaks of two compounds was performed. It was found that VAR and DAC were resolved on X.O./PGE with different potentials at 1.4 V and 0.9 V, respectively using Britton-Robinson buffer (pH 2.2) and 0.1 molL⁻¹ KCl as a supporting electrolyte. In addition, with the aid of cyclic voltammetry, a mechanistic scheme for the oxidation behaviour of both VAR and DAC was suggested. The proposed square wave voltammetric method was successfully applied for trace quantification of VAR and DAC in male rabbits. The suggested approach shows detection and quantification limits in rabbit plasma samples of 0.06 and 0.17 μmolL⁻¹, respectively for VAR and 0.13 and 0.39 μmolL⁻¹, respectively for DAC. The pharmacokinetic parameters of VAR alone and in combination with DAC after oral administration to rabbits were successfully estimated. The obtained results confirm that when DAC is co-administered with VAR, plasma concentration of VAR increases, which necessitates dose adjustment for VAR to prevent toxicological consequences in patients.

Keywords:

Square wave voltammetry, Vardenafil hydrochloride, Daclatasvir dihydrochloride, Xylenol orange, Pharmacokinetic study, Rabbit plasma.

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