Comparative pharmacokinetic study of Ledipasvir after single dose using novel methodology

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Background: Ledipasivir (LEDV) is a direct acting antiviral used for treatment of hepatitis C, especially in GT4 infection via termination of HCV proliferation inside the body and has the advantage of dose reduction compared to the other traditional antiviral agents. Dose adjustment is highly important for improving the efficacy of therapy and decreasing both the side effects and patient health's care cost. To obtain clinically trusted data, we should use highly sensitive and selective bio-analytical techniques, capable of using small sample volumes, with no interferences from endogenous or exogenous compounds.

Aim of work: Therefore, pharmacokinetic study of LEDV was investigated using novel validated highly sensitive sensor obtained in our laboratories and comparing the results with the reported results obtained by using LC/MS/MS technique.

Method: Six volunteers had fed prohibited for 12 h before the study but the water was freely available. The blood samples (3.0 mL) were collected from a forearm vein into heparinized polyethene tubes at 0.00 (pre-dose), 0.5, 1.0, 1.5, 2, 2.5, 3, 3.5, 4, 6, 10, 13, 18, 24 h after oral administration of Harvoni®400/90 mg tablets. The samples were immediately centrifuged at 4000 rpm for 10 min. The plasma was stored at −80ºC until analysis. The pharmacokinetic parameters for LEDV were estimated using the validated moment analysis software.

Results: The methodology was fully validated according to FDA guidelines with respect to linearity, accuracy, precision, recovery, selectivity. The sensitivity of the method was found to be sufficient for accurately measuring the main pharmacokinetic parameters for LEDV. The validated methodology was successfully applied to determine LEDV in human plasma after oral administration of a tablet containing 400/90 mg SOF/LED. Following absorption, LEDV reaches maximum plasma concentrations (T max) at 4.23± 2.09 h post-dose and is eliminated with (t½) of 31.1± 2.6 h. The Cmax was 183.7± 25.6 ng/mL, while AUC 0-t and AUC 0-∞ were 3709±1033 and 4201± 2345 ng/mL.h, respectively. The elimination rate constant (Ke) and clearance (CL) were 0.026± 0.0001 h-1 and 0.034± 34.6 mg/(ng/mL h), respectively. Our study proved that there was no significant difference in pharmacokinetic parameters with other reported data.

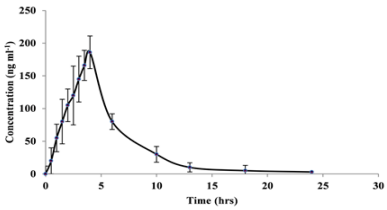

Figure 1. Mean plasma concentration of LEDV measured by RGO/ NS Ni Fe2O4/ MHS/GCE (±SD) using DPV at optimized conditions following administration of single oral dose of Harvoni® tablets.

Speaker Biography

Saad Alkahtani is currently Dean for College of Pharmacy at Najran University, Saudi Arabia. He is also an Associate Professor of Clinical Pharmacy, College of Pharmacy. Saad holds a PhD in Pediatric Clinical Pharmacology from the University of Nottingham, UK, 2013. He earned his Master's Degree from University of Glasgow, UK, 2009 and his undergraduate studies at King Saud University, Saudi Arabia, 1999. His research interest lies in evaluating cultural perceptions of, and access to healthcare and pharmacy services. His other research interests include pharmacoepidemiology and counterfeit medications. He has collaborated actively with researchers in several other disciplines of pharmaceutical sciences, particularly drug designing. He serves and has served in various committees at the Faculty. He is and has been a member of various national and international committees and working groups in the area of clinical pharmacy and pharmacy education. He has published many peer reviewed journal articles and conference papers and he is a reviewer for several international peer-reviewed journals.

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