ISSN: 2521-0815 (Print)
ISSN: 2521-0432 (Online)

Contents List available at RAZI Publishing
Matrix Science Pharma (MSP)
Journal Homepage: http://www.razipublishing.com/journals/matrix-science-pharma-msp/

# PHARMACOKINETIC STUDY OF CLARITHROMYCIN IN HUMAN FEMALE OF PAKISTANI POPULATION

**Atifa Mushtaq[1*], Tanweer Khaliq[1], Hafiz Alam Sher[2], Asia Farid[1], Anila Kanwal[1], Maliha Sarfraz[1]**

*[1] Institute of Pharmacy, Physiology and Pharmacology, University of Agriculture Faisalabad Pakistan*
*[2] Primary and Secondary Health Care Department, Lahore, Pakistan*
**Corresponding author email: atifa_mushtaq@yahoo.com*

**ARTICLE DETAILS**

***Article History:***

Received 12 May2017
Accepted 12 July 2017
Available online 21 September 2017

***Keywords:***

Pharmacokinetics,
Clarithromycin, HPLC, Plasma

**ABSTRACT**

The study was designed to assess the various pharmacokinetic parameters of a commercially available clarithromycin Tablet (Klaricid® 250 mg Abbot, Pakistan) in plasma sample of healthy adult female volunteers by applying a rapid, sensitive and accurate HPLC-UV analytical method. The human plasma samples were evaluated by using an isocratic High-Performance Liquid Chromatography (HPLC) system of Sykam consisted of a pump with a column C18 column (250×4.6mn, 5µm) UV-detector. The mobile phase comprises of potassium dihydrogen phosphate (50 mM, pH 6.8, contained 0.7% triethylamine), methanol and acetonitrile (30:25:45, v/v/v) was delivered with injection volume of 20µL at flow rate of 1 mL/min. The detection was performed at $\lambda_{max}$ 275 nm. By applying this method, important pharmacokinetic parameters $C_{max}$, $T_{max}$, Area under curve (AUC), half-life ($t_{1/2}$), Volume of distribution (Vd) and Clearance (Cl) were measured. The parameters of pharmacokinetics of clarithromycin were calculated by software (APO) pharmacological analysis. Maximum plasma concentrations $C_{max}$ 2.78 ±0.33 µg/ml, time to reach maximum concentration $t_{max}$ 2.82 ± 0.11 h and Area under curve AUC was 20.14h.µg/ml. The mean ± SD values obtained for the pharmacokinetic parameters showed a significant difference in pharmacokinetic parameters observed in previous literature which emphasizes the need for dose adjustment of clarithromycin in Pakistani population.

## 1. INTRODUCTION

Antibacteria Clarithromycin is semi-synthetic broad-spectrum macrolide antibiotic having both bactericidal and bacteriostatic activity [1].It is an acid stable drug showing better oral absorption, lower frequency of gastrointestinal intolerance and longer half-life [2].It is primarily metabolized to its biologically active 14-hydroxy-6-O-methyl erythromycin metabolite in both human and animal [3]. Clarithromycin kill bacteria by interrupting with their protein synthesis and bind reversibly to 50S ribosomal sub unit inhibiting translation and translocation of peptides [4].

The Asian countries have diverse environmental, topological and nutritional condition from west which ultimately affects the genetic makeup of man. As most of the drug literature is acquired from western countries so, Pakistan being an importer of raw and finished drugs must investigate the pharmacokinetic parameters by conducting different clinical and pre-clinical investigation [5]. Studies conducted on it shown the varied results of pharmacokinetics parameters under different indigenous condition as specified in literature. Pharmacokinetic studies provide essential data for the calculating dosage regimen of the drug. In an order to individualize the dose and to know the kinetics of drug in a specified environment, pharmacokinetics studies must be carried out. In most cases the genetic makeup of indigenous animals and environmental conditions are different from their foreign counterparts and this affects the biodisposition of drugs. So, evaluation of kinetic parameters in indigenous animal species and human is necessary [6].

The analytical methods stated earlier for the quantification of clarithromycin in biological fluids were microbiological bioassay and high-performance liquid chromatography (HPLC). Different HPLC methods have been developed for analysis of clarithromycin in human serum using Electrochemical, Mass Spectroscopy, fluorescent detection and UV [7]. Among all these UV detector is the most inexpensive commonly distributed and requiring only a small volume of biological sample [8]. The present study was designed to evaluate the pharmacokinetic variation and dose determination of clarithromycin in Pakistani population.

## 2.MATERIALS AND METHODS

### 2.1 Chemicals

Clarithromycin (Klaricid® 250 mg) was from Abbott Pharmaceutical Company (Pakistan). Certified reference materials (CRMs) of clarithromycin USP28 (984µg/mg) was supplied by Zhejiang Better Pharmaceuticals Co., Ltd., China. HPLC grade acetonitrile (ACN) and methanol (MeOH) were obtained from Fisher Scientific limited (New Jersey, USA). Analytical grade triethylamine (TEA) was kindly provided by Danas Pharmaceutical Islamabad. Potassium dihydrogen phosphate, ethyl ether, sodium hydroxide (NaOH), concentrated phosphate acid and dichloromethane ($CH_2Cl_2$) were obtained from Department of Physiology and Pharmacology, UAF, Faisalabad. Water was glass-double distilled and further purified for HPLC.

### 2.2 Instrumentation and chromatography

Chromatography was performed with a High-Performance Liquid Chromatograph (Sykam, S-1122) and analyses were determined using UV detector (Sykam, S-3210). A stainless-steel column packed with YMC pack A-312 (BDS-C18 with 250 x 4.6mm dimensions and 5µm particle size) was used. The output of the detector was monitored with computer software (Peak Simple Chromatography Data System, Buck Scientific Inc., East Norwalk). Analytical Balance (Sartorius, Germany). Centrifugation Machine (MSE Micro Centaur, Sanyo UK). Sonication apparatus (Oqawa seiki Co, Japan).

### 2.3 Study design

Eight healthy female volunteers were recruited to participate in this study. The average age was 22years (range18-26) and the average weight was 57kg range (45-70 kg). The study protocol was approved by the ethical committee at University of Agriculture Faisalabad. The nature of the study was explained to the volunteers and a written consent was obtained from each volunteer. All the volunteers had normal kidney and liver functions and were free from any chronic disease such as hypertension, diabetes, hypotension or liver

chromatography with electrochemical detection. Journal of chromatography, 783, 359-363.

[4] Zuckerman, J.M. 2004. Macrolides and ketolides: azithromycin, clarithromycin, telithromycin. Infectious disease of clinical north America, 18, 621-649.

[5] Javed, I., Rahman, Z.U., Khan, F.H., Muhammad, F., Iqbal, Z., and Aslam, B. 2006. Renal clearance and urinary excretion of kanamycin in domestic ruminants species. Pakistan Veterinary Journal, 26, 1-8.

[6] Ali, A., Afzal, S., Ashraf, M., Amin, S., Usman, M.J.A. 2012. Pharmacokinetic study of ketoprofen in healthy sheep under local conditions of Pakistan. The Journal of Animal and Plant Sciences, 22, 588-592.

[7] Bahrami, G., and Mohammadi, B. 2007. Determination of clarithromycin in human serum by high-performance liquid chromatography after pre-column derivatization with 9-fluorenylmethyl chloroformate: Application to a bioequivalence study. Journal of Chromatography, 850, 417–422.

[8] Forouten, S.M., Zarghi, A., Shafaati, A., Madadian, B., and Abolfathi, F. 2013. Rapid high-performance liquid chromatography method for clarithromycin in human plasma amperometry detection: Application in pharmacokinetic and bioequivalence studies. Iranian journal of pharmaceutical research, 12, 65-69.

[9] Steel, R.G.D., Torrie, J.H., and Dicke, D.A. 1997. Principles and procedures of statistics: A biometrical approach, 3rd Edition, McGraw Hill Book Co, 284-231.

[10] Shargel, L., and Yu, A. 1999. Applied Biopharmaceutics and Pharmacokinetics, 4th ed., Appleton & Lange, Stamford, 154-163.

[11] Alkhalidi, B.A., Tamimi, J.J., Salem, I.I., Ibrahim, H., and Sallam, A.A. 2008. Assessment of the bioequivalence of two formulations of clarithromycin extended-release 500-mg Tablets under fasting and fed conditions: a single- dose, randomized, open-label, two-period, two-way crossover study in healthy Jordanian male volunteers. Clinical therapeutics, 30, 1831-1843.

[12] Alffenar, J.W.C., Nienhuis, De Velde, F., Zuur, A.T., Wessels, A.M.A., Almeida, D., Grosset, J., Adjei, O., Uges, D.R.A., and Werf, T.S.V.D. 2007. Pharmacokinetics of rifampin and clarithromycin in patients treated for Mycobacterium ulcerans infection. Journal of antimicrobial chemotherapy, 54, 3878-3883.

[13] Madan, P.L. 2000. Biopharmaceutics and Pharmacokinetics, 1st ed., Jaypee Brothers Medical Publishers (P) Ltd., New Delhi, 406-494.

[14] Amini, H., and Ahmadiani, A. 2005. Sensitive determination of clarithromycin in human plasma by high-performance liquid chromatography with spectrophotometric detection. Journal of chromatography, 817, 193-197.

[15] Shin, J., Pauly, D.F., Johnson, J.A., and Frye, R.F. 2008. Simplified method for determination of clarithromycin in human plasma using protein precipitation in a 96-well format and liquid chromatography–tandem mass spectrometry. Journal of chromatography, 87, 130–134.