A STUDY OF PHARMACOKINETICS OF ANTI-TUBERCULOSIS DRUGS IN ZAMBIAN PTB PATIENTS CO-INFECTED WITH THE HUMAN IMMUNO-DEFICIENCY VIRUS.

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THIS DISSERTATION OF **DR. LAKHI SHABIR** IS APPROVED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE MASTERS DEGREE IN INTERNAL MEDICINE.

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To ROKAYA and SALIM

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ABBREVIATIONS INDEX

AIDS	Acquired Immune Deficiency Syndrome
ATT	Anti-Tuberculosis Treatment
ANOVA	Analysis of Variance
AUC	Area under the concentration versus time curve
CD4	Cluster Differentiation: T-helper/ inducer lymphocytes
CD8	Cluster Differentiation: T-helper/ inducer lymphocytes (Comprises 2/3 circulating T cells)
Cmax	Maximum measured Drug Concentration
CN	Cyanide
CSF	Cerebral Spinal Fluid
DOTS	Directly Observed Treatment Short Course
FBC	Full Blood Count
GIT	Gastro-intestinal Tract
HIV-1	Human Immune Deficiency Virus type 1
HIV-2	Human Immune Deficiency Virus type 2
HPLC	High Performance Liquid Chromatography
LFTs	Liver Function Tests
MDR-TB	Multi-Drug Resistance Tuberculosis
MIC	Minimum Inhibitory Concentration
PAS	Sodium *para*-aminosalicylate
PTB	Pulmonary Tuberculosis
RNA	Ribonucleic Acid
TB	Tuberculosis
TDM	Therapeutic Drug Monitoring RNA
UK	United Kingdom
USA	United States of America
UTH	University Teaching Hospital, Lusaka, Zambia
UV	Ultra Violet
WHO	World Health Organization
ZDHS	Zambia Demographic and Health Survey

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ABSTRACT

SETTING:

*The present study assesses the pharmacokinetic parameters for **rifampicin, isoniazid** and **pyrazinamide** in Zambian PTB patients with HIV at the University Teaching Hospital, Lusaka, Zambia. The assaying of the drugs was done at the University College London Medical School.*

OBJECTIVE:

To determine whether the pharmacokinetics of anti-tuberculosis drugs at steady-state are altered in HIV infected patients especially those with chronic diarrhoea.

METHOD:

*60 pulmonary tuberculosis patients, (20 HIV negative, 20 HIV positive without diarrhoea and 20 HIV positive patients with diarrhoea) were entered into a pharmacokinetic trial. Following supervised administration of standard doses of isoniazid, rifampicin and pyrazinamide, the plasma concentrations were measured over 24 hours to obtain the pharmacological parameters of the drugs. The following were then compared in the three groups for any significant difference: maximum measured drug concentration **(Cmax)** and area-under-the-concentration-time curve to 24 hours **(AUC).***

RESULTS:

No notable differences emanated between the three groups i.e. HIV negative, HIV positive without and with chronic diarrhoea, on comparing the Cmax and AUC ($P>0.05$). 20% of the participants were found to be fast acetylators (extrapolated using $t_{1/2}$ for isoniazid).

CONCLUSION:

This study could find no conclusive evidence that HIV infection, especially associated chronic diarrhoea affected the pharmacokinetics of the anti-tuberculosis drugs.