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AN EXPERIMENTAL STUDY TO COMPARE OUTCOMES BETWEEN ANIMALS & HUMAN AFTER SINGLE ISONIAZID (INH) ORAL DOSE TO TREAT VARIOUS INFECTIONS

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Abstract:
Objective: *Research objective was the investigation of isoniazid bio-disposition in the "Teddy Goats".*
Material and Methods: *Our experimental research was carried out at Sir Ganga Ram Hospital, Lahore in coordination with agriculture university from March, 2016 to January, 2017 in order to investigate the isoniazid (INH) Bio-disposition after the administering of single oral dose at (10 mg / Kg) according to the body weight of the Teddy goats. Each animal was drained for blood sample at pre-determined interval form the time of oral dose administration. Isolation of plasma was made through centrifuge process and it was analyzed through spectrophotometer for INH.*
Results: *Concentration Vs profile of time of every goat was used for the INH bio-disposition determination. Two compartments were used for the description of the data; open pharmacokinetic (PK) model and numerous parameters of the PK were measured and those were observed non-comparable with the available literature.*
Conclusions: *On the basis of the research outcomes we can conclude that imported antimicrobial drugs disposition studies are to be conducted in the presence of native conditions in order to make them rational with the regimen of dose in the local species of the animals.*
Keywords: *Isoniazid, Bio-disposition, Teddy goats and Spectrophotometer.*

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INTRODUCTION:

Baldan is of the view that various infections are well treated and managed though antibiotics in domestic animals and human beings [1]. Lees opines, to treat the microbial infection, antibacterial drug effective concentration is essential which is to be attained rapidly with infection and its maintenance in the appropriate time [2]. There is a variation in the achieved concentration with drug systemic availability, dosage, dosing rate, administration routes and access ability to site of the infection. There also variations in the concentration depending upon the physicochemical drug characteristics, which is influential on the absorption extent, distribution patterns and elimination of the mechanisms such as pharmacokinetic features. Microbial susceptibility to concentration of the drug is another aspect which is critical in the antibiotic clinical efficacy. Javed wrote; thus, an effective therapy is dependent on the bacterial susceptibility triad, drug's pharmacokinetic features and rate of the drug dose [3].

From the time of its initial introduction the INH has been the first choice of the healthcare providers in order to treat tuberculosis prophylaxis [4]. INH, for the resting bacilli it is considered as bacteriostatic; whereas, it is bactericidal for the speedy microorganism's divisions. It can treat the induced tuberculosis for experimental purposes in the animals. Cell penetration is easy and it effectively handles the growth of bacilli [5]. This kind of research has not been conducted at local level in order to study INH bio-disposition. As the use of INH is common in the animals so we planned to conduct a research on the investigation of isoniazid bio-disposition in the "Teddy Goats".

MATERIAL AND METHODS:

Our experimental research was carried out at Sir Ganga Ram Hospital, Lahore in coordination with agriculture university from March, 2016 to January, 2017 in order to investigate the isoniazid (INH) Bio-disposition after the administering of single oral dose at (10 mg / Kg) according to the body weight of the Teddy goats. Each animal was drained for blood sample at pre-determined interval form the time of oral dose administration. Isolation of plasma was made through centrifuge process and it was analyzed through spectrophotometer for INH.

Age and weight of the subjects was respectively (1 – 3 years) and (20 – 40 kg). All the subjects were clinically healthy and identical management was extended to all of them during the research timeframe such as (fresh green food, libitum and water). Dose administration was made orally (one percent INH syrup @ 10mg / kg) in order to research drug PK (pharmacokinetics).

Collection of blood samples was made through jugular vein by using disposable syringe (strict aseptic conditions applied); blood was transferred to centrifuge tubes for laboratory assessments. Sample collection was made at various intervals after the drug administration; centrifugal process was carried out @ 4000 revolution per minute for a time of fifteen minutes and kept at a temperature of (– 20° C).

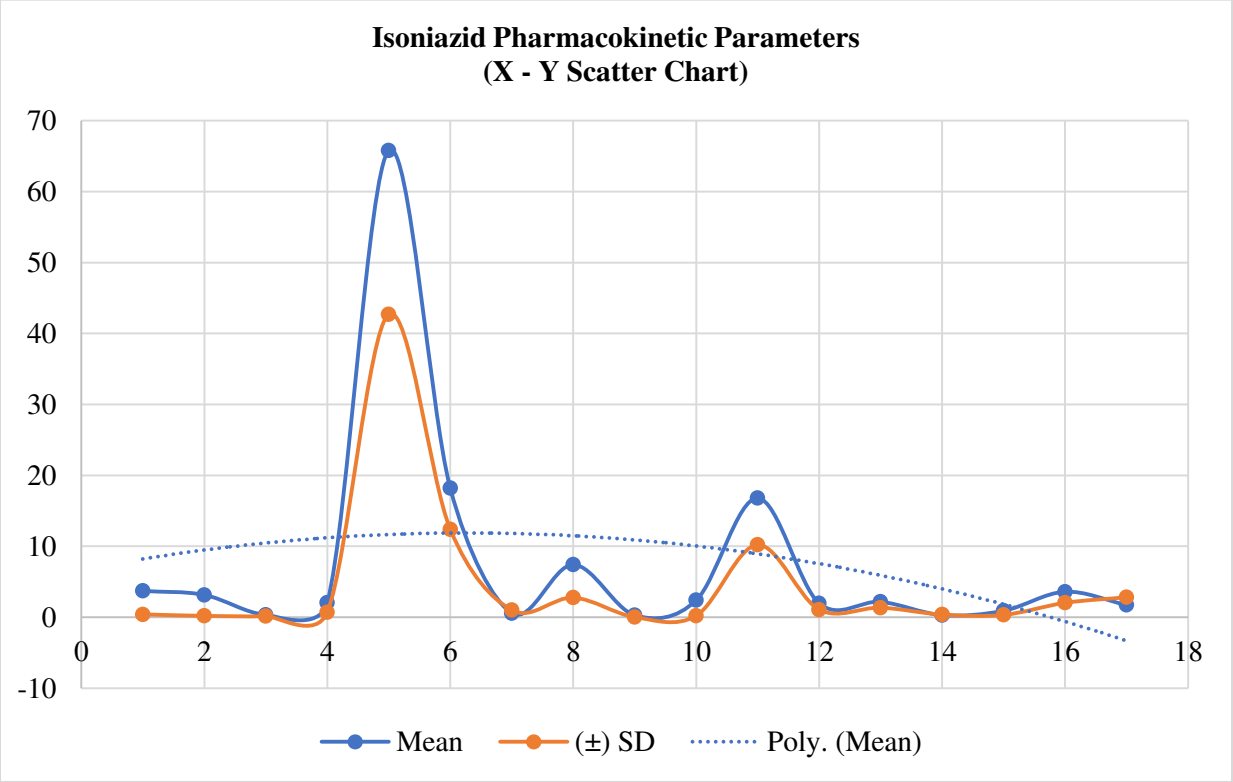
Spectrograph was used for the determination of the concentrations of INH in the plasma samples of all subjects INH concentrations in plasma samples [6 – 7]. Various PK parameters were calculated through the time data and concentrations of plasma by using a pharmacokinetic software. Under the curve area is calculated through this trapezoidal technique. Correlation coefficient and regression analysis (Least Square) was also taken.

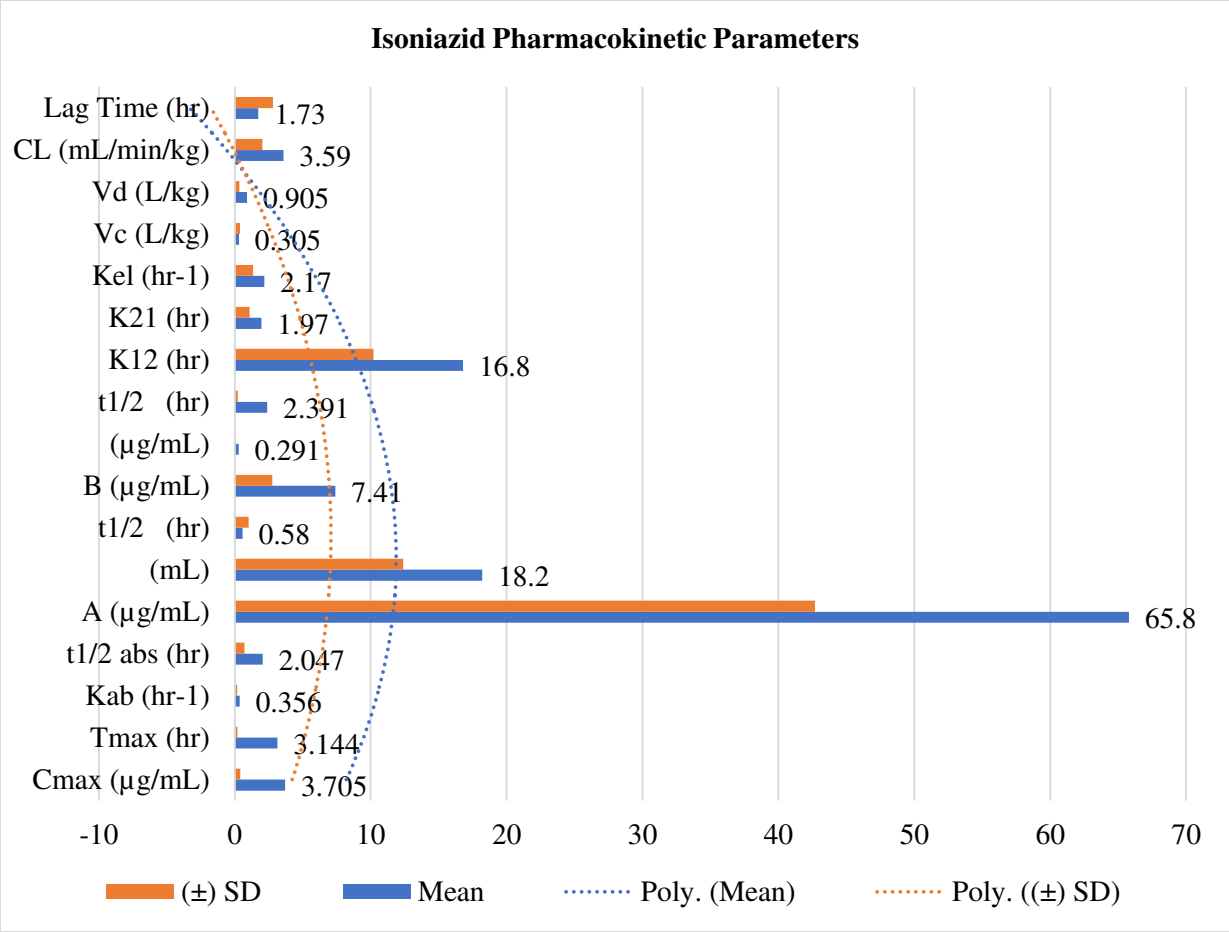
RESULTS:

Concentration Vs profile of time of every goat was used for the INH bio-disposition determination. Two compartments were used for the description of the data; open pharmacokinetic (PK) model and numerous parameters of the PK were measured and those were observed non-comparable with the available literature. Detailed outcomes analysis of Mean and SD values have been carried out in the given table about INH and PK parameters in the given subjects.

Table1: Mean ± SD values of pharmacokinetic parameters of isoniazid after oral administration in eight Teddy goats.

Isoniazid Pharmacokinetic Parameters	Mean	(±) SD
C max (µg/mL)	3.705	0.403
T max (hr)	3.144	0.193
Kab (hr-1)	0.356	0.163
t1/2 abs (hr)	2.047	0.72
A (µg/mL)	65.8	42.7
(mL)	18.2	12.4
t1/2 (hr)	0.58	1.01
B (µg/mL)	7.41	2.76
(µg/mL)	0.291	0.024
t1/2 (hr)	2.391	0.216
K12 (hr)	16.8	10.2
K21 (hr)	1.97	1.08
Kel (hr-1)	2.17	1.35
Vc (L/kg)	0.305	0.373
Vd (L/kg)	0.905	0.327
CL (mL/min/kg)	3.59	2.03
Lag Time (hr)	1.73	2.81





DISCUSSION:

After the oral administration of the INH dose we achieved peak concentration of the plasma "C max" as (3.79±0.335) µg/mL, which was achieved after two and a half hours. The concentration of the plasma at an interval of one hour was noticed at the same dose as (2.43±0.398) µg/mL; which was higher in terms of P-value (< 0.05) in comparison to the (1.85±1.6) µg/mL when compared with the human samples for the treatment of same disease [8]. This variation may be attributed to species difference or it can be attributed to the environmental variations [9]. In the course of present research. INH's "C max" in goats in terms of "T max" was greater than as observed in human beings respectively at an interval of 2.5 and 1.5 hours [5]. Following a 200 md INH dose in the healthy subjects the rage of "T max" was from (1 – 2) hours and range of the "C max" was (8.5 – 15) mg/L [10]. However, according to Jayaram at a dose of 120 mg, "T max" was in the range of (0.16 – 0.5) hours [11]. Difference in the species is the major cause of the variations because the stomach of the human is simple; whereas, goats have a compound stomach that has its effect on the process of absorption.

Walubo conducted his research on the rabbits and observed higher values of "Vd" in comparison to our research respectively as observed in our research was (0.905±0.327) L/kg which was lower than the outcomes of Walubo (4.29±1.25) & (3.02±0.55) L/kg observed through oral and IV "intravenous" INH dose administration [12]. This reflects the penetration of the tissue by the administrated drug in these research studies. However, humans have been reported with a reduced "Vd" value such as (0.6 L/kg) after the administering of single INH dose administration (Boxenbaum, 1974). This variation of the "Vd" value may be attributed to the variation in species, weight and age.

A short half-life reflects rapid drug elimination and delayed elimination is displayed by the long half-life from the body of human and animals. INH half-life values as observed in this research were recorded at a dose of ten milligrams per kilogram of body weight (2.39±0.216) hours; which can be compared to almost similar value as observed by Thomas on a

research conducted on rabbits with the administration of fifty milligrams per kilograms of the body weight as (2.67±0.36) hours (1981).

CONCLUSIONS:

On the basis of the research outcomes we can conclude that imported antimicrobial drugs disposition studies are to be conducted in the presence of native conditions in order to make them rational with the regimen of dose in the local species of the animals.

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