International Journal of Multidisciplinary Research And Studies

Available online at https://ijmras.com/

INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH AND STUDIES
ISSN: 2640 7272
Volume: 04.; Issue: 11/ 2021

Page no.- 06/06

NANOPARTICLE FOR SUSTAIN RELEASE OF ACYCLOVIR INVITRO AND INVIVO DRUG COMPARTMENT MODELLING

Mahendra Singh Kushwah[1]

[1]*Masters in Pharmaceutical Science from University Of Rajiv Gandhi Proudyogiki Vishwavidyalaya Bhopal (MP), India*

ARTICLE INFO

Corresponding Author:

Mahendra Singh Kushwah[1]

[1]*Masters in Pharmaceutical Science From University Of Rajiv Gandhi Proudyogiki Vishwavidyalaya Bhopal (MP), India*

mahendrasingh.9276@gmail.com

ABSTRACT

The main objective of this study was to organize the In-Vitro and In-Vivo correlation of immediate release Acyclovir tablets of 800 mg. In vitro and in vivo studies are done on the test product as Acyclovir Tablet USP 800 mg (containing Acyclovir 800 mg) of Cadila Medicinals Ltd., India versus Zovirax Tablet 800 mg (containing Acyclovir 800 mg) of GlaxoSmithKline, USA. In vivo studies are done in 36 healthy, adult, mortal subjects under fasting conditions. In vitro dissolution study was done using USP outfit II at 50 rpm in0.1 N HCL for 45 twinkles. The in vitro – in vivo interdependence of Acyclovir shows R- squared value of0.9794 in the excel worksheet, which depicts a successful correlation between in vitro and in vivo Characteristics of the medicine. In addition, PE AUC and PE C-max were plant to be –4.604 and-11.19 independently for each expression. The present study shows a good correlation between in vivo and in vitro PK biographies of the expression used as the test medicine in the study.(12)

KEYWORDS: Acyclovir 800 mg tablets, In Vitro Dissolution, In Vivo absorption, IVIVC, C-max, cpk, pk

I. INTRODUCTION

In vitro in vivo interdependence plays a crucial part in the medicine development and optimization of the expression is an integral part of manufacturing and marketing which is clearly a time- consuming and precious process. In vitro-in vivo interdependence (IVIVC) demonstrates the direct connections between in vitro dissolution/ release and in vivo immersion biographies. The in vitro property generally is the rate or quantum of medicine dissolution or release, while in vivo response in tube medicine attention or quantum of medicine absorbed. (1) The in vitro release data of a lozenge form containing the active substance serve as characteristic in vitro property, while the in vivo performance is generally represented by the time course of the tube attention of the active substance. These In vitro & In vivo data are also treated scientifically to determine correlations. For oral lozenge forms, the in vitro release is generally measured and considered as dissolution rate. The relationship between the in vitro and in vivo characteristics can be expressed mathematically by a direct or nonlinear interdependence. Still, the tube attention cannot be directly identified to the in vitro release rate; it has to be converted to the in vivo release or immersion data, either by pharmacokinetic cube model analysis or by direct system analysis. Different IVIVC proto-type are used as a tool for expression development and evaluation of immediate and extended-release lozenge forms

for setting a dissolution specification and as a surrogate for bioequivalence testing. Virtually, the purpose of IVIVC is to use medicine dissolution results from two or further products to prognosticate similarity or diversity of anticipated tube medicine attention (biographies). Before one think of relating in vitro results to in vivo, one has to build similarity or diversity of in vivo response i.e. tube medicine attention biographies. As a result, considerable trouble goes into their development and the main outgrowth is "the capability to prognosticate, directly and precisely, anticipated bioavailability characteristics for an extended-release (ER) medicine product from dissolution profile characteristics. [2, 3] The methodology of establishing similarity or diversity of tube medicine attention profile is known as bioequivalence testing. There are veritably well-established guidance's and norms available for building bioequivalence between medicine biographies and products [4, 5]. There are four situations of IVIVC that recount within the FDA guidance, which include situations A, B, C, and multiple C [6, 2]. The conception of interdependence position is grounded upon the capability of the interdependence to reflect the complete tube medicine position- time profile which will affect from administration of the given lozenge form. An IVIVC Level A correlates the entire in vitro and in vivo biographies has nonsupervisory applicability. This position of interdependence is the loftiest order of interdependence and represents a point-to-point relationship between in vitro dissolution rate and in vivo input rate of the medicine from the lozenge form [8]. [12]

This ideal should guide the choice and interpretation of evaluation styles. Any applicable approach related to this ideal may be used for evaluation of predictability prediction crimes are estimated for C-max and AUC to determine the validity of the interdependence. Colorful advancements are wont to evaluate the magnitude of the error in privies the in vivo bioavailability results from in vitro dissolution data [8, 9]. It can be calculated by Vaticination error that's the error in vaticination of in vivo property from in vitro property of medicine product. Depending on the intended operation of an IVIVC and the remedial indicator of the medicine, evaluation of vatic nation error internally and/ or externally may be applicable. [5][12]

Acyclovir may be a synthetic purine nucleoside analogue with in vitro and in vivo inhibitory exertion against herpes simplex contagion types 1 (HSV-1), 2 (HSV-2), and varicella-zoster contagion (VZV). This viral enzyme changes Acyclovir into Acyclovir mono-phosphate, a nucleotide analogue. In vitro, Acyclovir tri-phosphate stops modification of herpes viral DNA. The lesser antiviral utilization of Acyclovir against HSV in contrast to VZV is due to its more effective phosphor rylation by the viral TK [10]. Acyclovir pharmacokinetics has been considerably delved during the colorful phases of clinical development. Utmost of the administered medicine is excluded from the body unchanged, via the feathers by glomerular filtration and tubular stashing. After intravenous dosing of cases with normal renal function, 8 to 14 of the cures is recovered in the urine as the metabolite 9-carboxymethoxymethylguanine. After oral administration, the bioavailability of Acyclovir was roughly 20. The tube elimination half-life of acyclovir is2.5 to3.3 hr and protein list is 9-33 [11].[12]

MATERIALS AND METHODS

Materials:

All accoutrements used for analysis were of logical grade. The test product for In Vivo study used Acyclovir Tablet USP 800 mg of Cadila MedicinalsLtd., India reference product used was Zovirax Tablet 800 mg of GlaxoSmithKline.[12]

IN VITRO EVALUATION:

The dissolution of Acyclovir tablets was carried out using USP Type II Dissolution outfit for 45 twinkles. The dissolution media used was 900 ml 0.1 N HCL at 37ºC ±0.5 ºC and rotated at a speed of 50 rpm. Analysis of the withdrawn samples was carried out using UV

Mahendra Singh Kushwah[1]; *[1]Masters in Pharmaceutical Science From University Of Rajiv Gandhi Proudyogiki Vishwavidyalaya Bhopal (MP), India ;* *mahendrasingh.9276@gmail.com.*

spectrophotometer at the maximum 254 nm against0.1 N Hydrochloric acid as a blank. (12)

DISSOLUTION PROCEDURE

Parameters of the instrument were set as mentioned over and the medium was degassed previous to use. 900 ml of Dissolution media was transferred into each of the six dissolution vessels and outfit was operated as per demand. One tablet was dropped into each of six different vessels & dissolution outfit was started incontinently. After 45 min result was withdrawn, & filtered the result through what mann sludge paper No. 1; relinquish first 2-3 ml of the filtrate. One mL of the filtered sample was adulterated to 100 ml with dissolution medium and mixed (Use this result as sample medication).(12)

PROCEDURE FOR ANALYSIS

Absorbance was measured for the standard medication and sample medication on a suitable spectrophotometer at the maximum 254nm against0.1 N Hydrochloric acid as a blank. The chance of Acyclovir dissolved in 45 twinkles in individual tablets was calculated. In vivo Immersion study A randomized, open- marker, two-treatment, two- period, two-sequence, two- way crossover relative bioavailability study of a single oral cure of Acyclovir Tablet USP 800 mg (containing Acyclovir 800 mg) of Cadila Medicinals Ltd., India versus Zovirax Tablet 800 mg (containing Acyclovir 800 mg) of 600 GlaxoSmithKline, USA in 36) healthy, adult, mortal subjects under fasting condition.(12)

SCREEN PROCEDURE

During screening procedure Demography data, standard physical examination with Vital signs, Clinical laboratory tests on blood and urine samples, Electrocardiogram (ECG) and Casket mX-ray were done. (12)

STUDY DESIGN

A randomized, open- marker, two-treatment, two- period, two- sequence, two- way crossover, relative bioavailability study, during which subjects were administered a single cure of test or reference product under fasting circumstances with at least 7 days washout period between each administration. (12).Sample Size: Minimum of 36 (04 buttress) healthy, adult, subjects was enrolled to allow dosing in both ages(12)

BIO-ANALYSIS OF TUBE SAMPLE

Samples were anatomized for the quantification of Acyclovir in tube using Liquid Chromatography with Mass Spectrometry (LCMS) procedures. Data examination was carried out using Win-Nonlin software to get the Cmax, AUC 0-t, AUC 0-and kel. (12)

STATISTICAL ANALYSIS

Statistical analysis was performed on the pharmacokinetic parameters data gain from subjects (Completing both the ages) using the SAS Statistical Software interpretation9.1.3 (SAS Institute INDIA Pvt. Ltd). (12)

IN-VITRO DISSOLUTION

The mean percent dissolved is calculated on the base of time and it showed that within the first 15 min,91.0 of Acyclovir medicine and within the first 20 min, 89 of Zovirax had dissolved. It was observed that96.0 of acyclovir and Zovirax dissolved within 45 min. Percent dissolved versus in vitro dissolution time (in min) when colluded generates a dissolution profile wind as shown below in table 1. The quantum of medicine dissolved over a period of time for test & reference expression is given in the figure 1. (12)

IN-VIVO ABSORPTION

The bit of medicine absorbed was calculated by Wagner Nelson system using following equation. Above equation relates the accretive quantum of medicine absorbed after a certain time to the quantum of medicine absorbed. The bit of medicine absorbed calculated using Wagner Nelson system for test & reference

Mahendra Singh Kushwah[1]; *[1]Masters in Pharmaceutical Science From University Of Rajiv Gandhi Proudyogiki Vishwavidyalaya Bhopal (MP), India ; mahendrasingh.9276@gmail.com.*

$$\frac{(X_A)_T}{(X_A)_\infty} = \frac{CT + K\int_0^T Cdt}{K\int_0^\infty Cdt}$$

Expression is epitomized in the Table 2. The following figure 2 and figure 3 summarizes the bit of medicine absorbed of the Acyclovir patch Test and reference independently at given blood slice time points for test medicine. It shows that at 1 hr nearly 90% of the medicine was absorbed for both test & reference expression. (12)

DETERMINATION OF INTENSITY FACTOR

Since the in vitro dissolution data was available only for one hour and hence a time spanning factor (i.e., intensity factor) was calculated using Rate of time of 90% absorbed and 90% dissolved & Rate of time of 50% absorbed and 50% dissolved. (12)

IN-VIVO OBSERVED DATA

With the help of time spanning factor, the in vitro data was compared with In vivo data. Table 3 summarizes bit of medicine absorbed & percent medicine absorbed vs. time data of Zovirax 800 mg tablets attained using Wagner Nelson Method. (12)

DEVELOPMENT AND EVALUATION OF LEVEL AN IVIVC MODEL

The in vitro data was taken grounded on twinkles and the in vivo immersion grounded on hours. It was apparent that these two processes passed over different time scale. To make the time difference between in vitro and in vivo data, livery, a time spanning factor (intensity factor) was calculated. The intensity factor, I, attained was 6.66. Therefore, by using this factor we've converted the in vitro time points to hours in order to match with the in vivo time points. Time gauged normalization of in vitro and in vivo data with intensity factor is given in figure 4. (12)

CORRELATION CALCULATION

The correlation graph (Figure 5) was colluded as absorbed verses dissolved and there exists an extremely good correlation of expression between in vitro and in vivo data. (12)

PREDICTION ERROR

IVIVC model pungency was determined by the calculating percent C-max and AUC vaticination crimes. Vaticination error as PE, AUC and PE C-max was plant to be –4.604 and-11.19 independently for each expression. An IVIVC should be estimated to demonstrate that pungency of in vivo performance of a medicine product from its in vitro dissolution characteristics is maintained over a range of in vitro dissolution rates and manufacturing process. However, surfactants, bibulous pressure, if in vitro dissolution is shown to be independent of dissolution conditions similar as PH. To demonstrate a correlation, bit absorbed in vivo should be colluded against bit dissolved in-vitro. However, also angles are super imposable, and there's a 11 relationship which is defined as point-to- point or Position a correlation, if this relationship becomes direct with a pitch of 1. Retrogression analysis was also performed on Excel spread distance with the same in vitro and in vivo data. R- Squared value attained from graph was0.9794. According to FDA guidelines and moxie, statistic from Level A analysis is r, the correlation measure. Its forecourt, i.e. R- squared, ranges from 0 to 1 and is a measure of strength of relationship between fragments absorbed against bit dissolved. Frequently, results with sufficient large R- squared (e.g., lesser than0.9) yielded "a successful interdependence". The in vitro – in vivo correlation of Acyclovir shows R- squared value0.9794 in excel work distance, which depicts a successful interdependence between in vitro and in vivo Characteristic of the medicine. In a direct interdependence, in vitro dissolution and in vivo input angles may be directly super imposable or may be made to be super imposable by the use of applicable scaling factor (time corrections). In addition, the PE for each expression shouldn't exceed 15.

Mahendra Singh Kushwah[1]; *[1]Masters in Pharmaceutical Science From University Of Rajiv Gandhi Proudyogiki Vishwavidyalaya Bhopal (MP), India ;* *mahendrasingh.9276@gmail.com.*

Then PEAUC and PE C-max was plant to be –4.604 and-11.19 independently. (12)

CONCLUSION

The present study shows a good correlation between in vivo and in vitro PK biographies of the expression used as the test medicine in the study. The in vitro – in vivo interdependence of Acyclovir shows an R- squared value of0.9794 in the excel worksheet, which depicts a successful correlation between in vitro and in vivo Characteristics of the medicine. In addition, PE AUC and PE C-max were plant to be –4.604 and-11.19 independently for each expression. The conception of interdependence position is grounded upon the capability of the correlation to reflect the complete tube medicine position- time profile which will affect from administration of the given lozenge form. An IVIVC Level A correlates the entire in vitro and in vivo biographies has nonsupervisory applicability. This position of interdependence is the loftiest order of interdependence and represents a point-to- point relationship between in vitro dissolution rate and in vivo input rate of the medicine from the lozenge form. (12)

TABLE 1: *IN VITRO* DISSOLUTION DATA OF ACYCLOVIR 800 MG TABLETS (TEST) AND ZOVIRAX 800 MG TABLETS (REFERENCE)

	0.1 N HCl	
Time (min)	Acyclovir 800 mg (test) Tablets	Zovirax 800mg (Reference) tablets
0	0	0
10	86	74
15	91	81
20	94	89
30	95	94
45	96	96

TABLE 2: FRACTION OF DRUG ABSORBED FOR TEST & REFERENCE

Fraction of Drug Absorbed		
Time (hr)	Test	Reference
0	0	0
0.333	0.208509	0.283505
0.667	0.600566	0.809927
1	0.902686	0.99656
1.333	1.086002	1.195828
1.667	1.187093	1.321714
2	1.13907	1.327762
2.5	1.173928	1.330732
3	1.257711	1.281141
4	1.137136	1.175827
5	1.067112	1.088926
6	0.956591	0.981582
8	0.886052	0.901321
10	0.851755	0.878418
12	0.835008	0.851137
14	0.841072	0.844374
16	0.852433	0.850673
24	0.876586	0.875232

TABLE 3: Fraction of Drug Absorbed

Time (hr)	Fraction drug absorbed	% Drug absorbed
0	0	0
0.333	0.283505	28.3505
0.667	0.809927	80.9927
1	0.99656	99.656
1.333	1.195828	119.5828
1.667	1.321714	132.1714
2	1.327762	132.7762

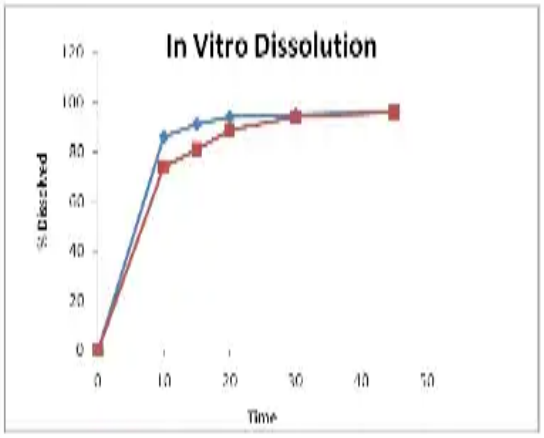

FIGURE 1: FRACTION OF DRUG DISSOLVED VS TIME GRAPH FOR ACYCLOVIR 800 MG TABLETS

Mahendra Singh Kushwah[1]; [1]*Masters in Pharmaceutical Science From University Of Rajiv Gandhi Proudyogiki Vishwavidyalaya Bhopal (MP), India ;* *mahendrasingh.9276@gmail.com.*

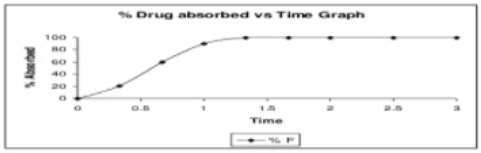

FIGURE 2: FRACTION OF DRUG ABSORBED VS TIME GRAPH FOR ACYCLOVIR 800 MG TABLETS (TEST)

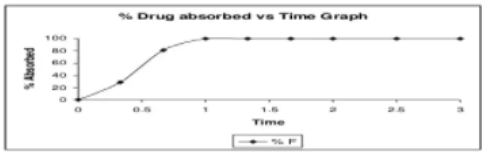

FIGURE 3: FRACTION OF DRUG ABSORBED VS TIME GRAPH FOR ZOVIRAX 800 MG TABLETS (REFERENCE)

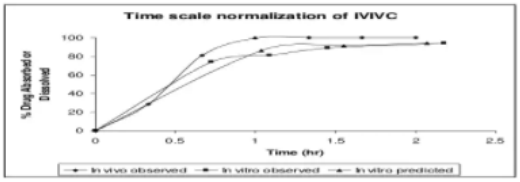

FIGURE 4: TIME SCALED NORMALIZATION OF *IN VITRO* AND *IN VIVO* DATA WITH INTENSITY FACTOR

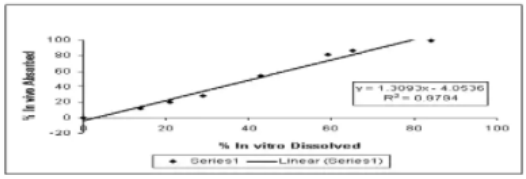

FIGURE 5: THE LINEAR REGRESSION PLOT OF % ABSORBED AND % DISSOLVED

REFERENCES

1. Leeson L. J. Drug Information Journal, 1995; 29: 903-915.

2. Gaynor C, Dunne A, Davis J., International Biometric Society, http://ibc2008abstracts.tibs.org/Other/IBC2008_Paper_ref_466.pdf

3. Modi NB, Lam A, Lindemulder E, Wang B, Gupta SK. Biopharm Drug Dispos, 2000; 21:321-326

4. Uppoor VRS. J Control Rel. 2001; 72:127-132.

5. Chilukuri DM, Sunkara G. Drug Delivery Technology, 2003; 3:4

6. Sirisuth N, Eddington ND, Int. J. Generic Drugs, 2002; Part 3:250-258.

7. Qureshi SA, The Open Drug Delivery Journal, 2010; 4: 38-47.

8. Jaber E. J. Pharm Pharmaceut Sci, 2006; 9 (2): 169-189.

9. Jayaprakasam B, Seeram NP, Nairs MG. Cancer Lett, 2003; 189 (1): 11-6.

10. www.rxlist.com

11. http://www.drugs.com/pdr/ Zovirax Tablets.html

12. Source https://www.slideshare.net/bhaswatchakraborty/ivivc-acyclovir

Mahendra Singh Kushwah[1];[1]*Masters in Pharmaceutical Science From University Of Rajiv Gandhi Proudyogiki Vishwavidyalaya Bhopal (MP), India ;* *mahendrasingh.9276@gmail.com.*