WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 05, 621-638. Research Article ISSN 2277–7105

FORMULATION AND EVALUATION OF SOLID DISPERSION INCLUDE FAST DISSOLVING TABLETS OF TENOFOVIR DISOPROXIL FUMARATE.

Sathya Surya Prasad Ch.[1*], J. Vijaya Ratna[1] and M. Mohanvarma[2]

[1]Division of Pharmaceutical Technology, AU College of Pharmaceutical Sciences, Andhra University, Vishakhapatnam-530003, Andhra Pradesh, India.

[2]Division of Pharmaceutical Technology, Shri Vishnu College of Pharmacy, Bhimavaram, West Godavari, Andhra Pradesh, India.

Article Received on
07 Jan. 2018,
Revised on 28 Jan. 2018,
Accepted on 17 Feb. 2018
DOI: 10.20959/wjpr20185-10824

***Corresponding Author**
Sathya Surya Prasad Ch.
Division of Pharmaceutical Technology, AU College of Pharmaceutical Sciences, Andhra University, Vishakhapatnam-530003, Andhra Pradesh, India.

ABSTRACT

The present study was to formulate solid dispersion include fast dissolving tablet of Tenofovir disoproxil fumarate to improve the aqueous solubility, dissolution rate. Solid dispersion of Tenofovir disoproxil fumarate was prepared with PVP K30, PEG 6000 and Soluplus in different drug: carrier ratio using physical mixing, solvent evaporation and kneading methods. FT-IR, Differential scanning calorimetry, X-Ray diffraction and scanning electron microscopy were performed to identify the physicochemical interaction between drug and carriers. The optimized solid dispersion (Drug: Soluplus 1:0.5 ratio in kneading method) were further used to prepare fast dissolving tablet by direct compression method using Superdisintegrants such as sodium starch glycolate, Cross carmallose sodium and crospovidone. The pre-compression parameter of powder blends suggested good flow ability and compressibility. The prepared tablets were evaluated for thickness, hardness, friability, weight variation, drug content, wetting time, *in-vitro* disintegration time and dissolution studies. The F6 formula shows highest release of 100.32% in 30 mins.

KEYWORDS: Tenofovir disoproxil fumarate, Soluplus, sodium starch glycolate, direct compression method, fast dissolving tablet.

INTRODUCTION

Oral drug delivery formulation and technologies are mainly focused on the following areas of gastro intestinal tract (GIT). Various challenges associated with oral route include, 1. Pill-swallowing difficulty. 2. Irritant and unpalatable drugs are not given by this route 3. Gastrointestinal (GI) destruction of labile molecule. 3. Low levels of macromolecular absorption; absorption of drugs may be affected by food in the stomach. 4. Slow onset of action. 4. Very little control over release of the drug; non-specific delivery site & side effects. As oral drug delivery is simple, most convenient, safest, non-invasive and most economical, it continues to be the preferential route of administration and researchers are seeking ways to incorporate various technologies in oral formulations; even small improvements in drug delivery technology can make significant differences in enhancing patient compliance and drug bioavailability.The oral administration is the most preferred route due to various advantages including ease of ingestion, avoidance of pain and most importantly patient compliance. For many drug substances, conventional immediate release formulations provide clinically effective therapy while maintaining the required balance of pharmacokinetic and pharmacodynamics profiles with an acceptable level of safety to the patient. Fast dissolving release tablets have started gaining popularity and acceptance because they are easy to administer and lead to better patient compliance. Despite of phenomenal advances in the other route of administration, the unavoidable truth is that the oral drug delivery remains well preferred delivery route.

Fast Dissolving Tablets

The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients, is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Dispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people. Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapimelts, porous tablets, quick dissolving tablets etc. Fast dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva. The faster the

drug into solution, quicker the absorption and onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form. The advantage of mouth dissolving dosage forms are increasingly being recognized in both, industry and academics. Their growing importance was underlined recently when European pharmacopoeia adopted the term "Orodispersible tablet" as a tablet that to be placed in the mouth where it disperses rapidly before swallowing. According to European pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes. The basic approach in development of FDT is the use of Superdisintegrants like cross linked carboxymethyl cellulose (croscarmellose), sodium starch glycolate (Primogel, Explotab), polyvinylpyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet after putting on tongue, there by release the drug in saliva. The bioavailability of some drugs may be increased due to absorption of drug in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. More ever, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablet. The technologies used for manufacturing fast-dissolving tablets are freeze-drying, spray-drying, tablet moulding, sublimation, sugar-based excipients, tablet compression, and disintegration addition. As a result of increased life expectancy, the elderly constitute a large portion of the worldwide population today. These people eventually will experience deterioration of their physiological and physical abilities.

Criteria for Fast dissolving Drug Delivery System

1. Not require water to swallow, but it should dissolve or disintegrate in the mouth with in seconds.
2. Be suited with taste masking dosage form.
3. Have a pleasant mouth feel.
4. Leave minimum or no residue in the mouth after oral administration.

Salient Feature of Fast Dissolving Drug Delivery System

1. Rapid dissolution and absorption of the drug, which will produce quick onset of action.
2. Pregastric absorption can result in improved bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwanted effects.
3. An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.

4. Maintain the stability for longer duration of time.

Tenofovir disoproxil fumarate is a defective adenosine nucleotide that selectively inhibits the action of reverse transcriptase, while only weakly interfering with mammalian DNA polymerases α, β, and mitochondrial DNA polymerase γ. Tenofovir prevents the formation of the 5′ to 3′phosphodiester linkage essential for DNA chain elongation. A phosphor di ester bond cannot be formed because the Tenofovir molecule lacks an –OH group on the 3′ carbon of its deoxy ribose sugar. Once incorporated into a growing DNA strand, Tenofovir causes premature termination of DNA transcription. The drug is classified as a nucleotide analogue reverse transcriptase inhibitor (NtRTI). Reverse transcriptase is a crucial viral enzyme in retroviruses such as human immunodeficiency virus (HIV) and in hepatitis B virus infections.

MATERIALS AND METHODS

Tenofovir disoproxil fumarate was a gift sample form Hetero Drugs Limited, Hyderabad, India. β - Cyclodextrins, HP-β-Cyclodextrins are supplied from BMR Pharma, Hyderabad in India. PVP K30, PEG- 6000 and SOLUPLUS are supplied from BASF, Mumbai in India. Lactose, Talc, Magnesium stearate, SSG, CCS, Crospovidone is supplied from gift sample from M/S. Orchid Health Care, Chennai in India. And melt granulation method.

Pre – Formulation studies

Differential scanning calorimetry

Conventional DSC and MTDSC experiments were performed using DSC Q200 (TA Instruments, NJ, USA) with a refrigerated cooling assembly (RCS) and a modulated capability. The DSC cell was purged with 50 ml/min dry nitrogen, and the RCS was purged with 150 ml/min nitrogen. The DSC cell was calibrated for baseline using empty pans of matched weight and for temperature using three temperature standards (Cyclohexane, $T_m = 279.54^o$ K; indium, $T_m = 429.61^o$ K; tin $T_m = 504.93^o$ K). About 3–5 mg of samples was exposed to the desired heating rates from the desired starting temperature to above the melting point of TDF under dry nitrogen purging (50 ml/min) in hermetically sealed aluminum pans. The data was analyzed using Universal Analysis Software from TA Instruments, NJ, and USA.

X-ray Powder Diffraction

The X-ray Powder Diffraction (pXRD) solid-state pattern of TDF was measured with D8 Advance (Bruker, USA) using an online recorder (PM 8203A) and Lynx Eye is the detector. Radiations were generated from CuKα source and filtered through Ni filters with a wavelength of 0.154 nm at generator current of 20 MA and voltage of 35 KV. The instrument was operated over the 2θ range of 2–50° at a step size of 0.015°.

Scanning Electron Microscopy

Surface morphology was examined by JEOL JSM-6400 (Jeol Ltd., Tokyo, Japan) scanning electron microscope (SEM). The samples were coated with gold, using sputtering technique, and the gold-coated samples were viewed for surface topography in SEM at an acceleration voltage of 10 KV at ×150 and ×500 magnification.

FTIR Spectroscopy Studies

The neat drug, neat polymers and solid dispersions prepared *ex- situ* were examined by FTIR spectroscopy using Perkin-Elmer [model: Spectrum 65 (C85069), UK] in diffused reflectance mode. The 2 to 3 mg of samples was thoroughly mixed, triturated with potassium bromide (100 mg) and placed in the sample holder. The samples were scanned from 4,000 to 450 cm^{-1}. The recording conditions were resolution, 4.0; zero fitting, 2.0; sample scan, 16 and acquisition, single sided.

Table: 1 FT-IR Studies Comparison of Different Functional Groups with API.

S. No.	Functional groups	Band range
1	-OH stretching unbound	3600-3400
2	C-H stretching aromatic	850-700
3	C-H alkanes stretching	2900-2850
4	C=O acids stretching	1700-1750
5	C-Cl	540-760

Analytical method development

Assay method for Tenofovir disoproxil fumarate

HPLC based analytical method development for determining the assay of Tenofovir disoproxil fumarate formulations was done using Luna C18, (250mm x 4.6mm) 5µm particle size column. The mobile phase consisted of a mixture of Acetonitrile and Buffer in the ratio of 20:80.Samples was filtered through 0.45µ membrane filter paper. The 2996 photodiode array detector (PDA) was used to establish the peak purity. While flow rate was kept at 1.0 ml/min, the detection was performed at 260 nm. Identification of Tenofovir disoproxil

fumarate was made by equating its retention time and their respective UV spectra using a PDA detector.

Preparation of standard solution

The 6.17 mg of Tenofovir disoproxil fumarate working standard was weighed into a 100 ml volumetric flask. The 70 ml of diluent was added, sonicated to dissolve and diluted to the volume with the diluent.

Further 5ml of the above solution was diluted to 50 ml of diluent.

Preparation of sample solution

The 10 tablets were taken, the average weight was noted and then one tablet equivalent weight of 18.51 mg of sample was transferred into a 100 ml volumetric flask. The 70 ml of diluent was added, sonicated to dissolve and diluted to the volume with the diluent.

Further 5ml of the above solution was diluted to 50 ml with the diluent. The solution was filtered through 0.45µ Nylon syringe filter.

Procedure

Inject 10µl of standard preparation five times and sample preparation in the chromatograph. Record the chromatograms and measure the peak responses for Tenofovir disoproxil fumarate. The system suitability parameters should be met. From the peak responses, calculate the content of Tenofovir disoproxil fumarate in the sample.

$$= \frac{AT}{AS} \times \frac{\text{Std wt (mg)}}{100\text{ml}} \times \frac{5\text{ ml}}{50\text{ml}} \times \frac{100\text{ ml}}{\text{Wt taken}} \times \frac{50\text{ml}}{5\text{ml}} \times \frac{\text{(P) \% Potency of Std}}{100} \times 1000$$

(OR)

Assay (%): Assay (mg/tab) x 100 / LC

Where

AT= Average area count of Tenofovir disoproxil fumarate peak in the chromatogram of sample solution.

AS= Average area count of Tenofovir disoproxil fumarate peak in the chromatogram of standard solution.

P= Percent potency of Tenofovir disoproxil fumarate working standard on as is basis.

LC= Label claim of Tenofovir disoproxil fumarate in mg.

Table 2: Standard calibration curve for Tenofovir disoproxil fumarate.

Injection Volume	Standard Area
2.81	158220
7.03	437680
14.05	797626
28.10	1690342
35.13	2034217
42.15	2467367

Formulations of Tenofovir disoproxil fumarate tablets

Formulation of Tenofovir disoproxil fumarate fast dissolving tablets by using super disintegrants.

Tenofovir disoproxil fumarate fast dissolving tablets were prepared by direct compression method. According to the formula given in Table 6.1.1, all the ingredients were passed through 40# mesh sieve separately and collected. The powdered (D:HP-β-CD: Soluplus, 1:0.50:0.50) ternary complex, containing amount equivalent to 300 mg Tenofovir disoproxil fumarate, was mixed with the other excipients and compressed into tablets, after lubrication with magnesium stearate (2%), and talc (2%) by using 16 station rotary tablet compression machine equipped with 9 mm flat - faced punches. The tablet weight was adjusted to 900 mg.

Evaluation parameters

Hardness

Hardness of the tablets was tested using a Monsanto Hardness Tester. Five tablets from each batch were tested for hardness.

Thickness

Thickness of the tablets was determined using Vernier calipers. Five tablets from each batch were used, and an average value was calculated.

Friability

Friability of the tablets was determined in a Roche friabilator. Ten tablets were weighed initially (w_1) and placed in the friabilator that revolves at a speed of 25 RPM, dropping those tablets at a distance of six inches height with each revolution and rotated in the friabilator for 100 revolutions. After completion of rotations, tablets were dedusted and weighed (w_2). The percent loss in weight or friability (f) is calculated by using the formula.

$f = (w_1-w_2)/w_1 \times 100$

Weight Variation Test

Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of twenty tablets was calculated.

Wetting Time

A piece of tissue paper folded twice was placed in a small petridish (internal diameter = 6.5 cm) containing 6 ml of simulated 0.1 N HCl. A tablet was put on the paper, and the time required for complete wetting was measured. Six trials were performed for each batch and the average time for wetting with standard deviation was recorded.[19]

Drug Content Estimation

Ten tablets were taken and amount of drug present in each tablet was determined as follows: Tablet was crushed in mortar and transferred to a 100 ml flask. The powder was dissolved in pH 3.0.The sample was mixed by using Remi mixer for 5 minutes, after which it was filtered through what man's filter paper. The filtered solutions after appropriate dilution (1 to 10 ml) with 0.1N HCl buffer were analyzed by the validated UV spectrophotometric method at λ_{max} 260 nm.

***In-Vitro* Disintegration Time**

In -Vitro disintegration time was performed by apparatus specified in USP. The water was used as disintegration medium, and the temperature was maintained at 37±2°C and the time in seconds taken for the complete disintegration of the tablet, with no palpable mass remaining in the apparatus, was measured in seconds.

***In vitro* Dissolution Studies**

In-Vitro dissolution study was performed by using USP type II dissolution test apparatus (Paddle type) [Lab, India (DS-8000, Mumbai)] at 50 RPM. The 0.1N HCl, 900 ml was used as the dissolution medium which was maintained at 37±0.5^{o}C. Aliquots of dissolution medium (5 ml) were withdrawn at specific time intervals and were filtered. The amount of drug dissolved was determined by UV spectrophotometer by measuring the absorbance of the sample at 260 nm. Three trials for each batch were performed and average percentage drug release with standard deviation was calculated and recorded.[2]

RESULTS AND DISCUSSION

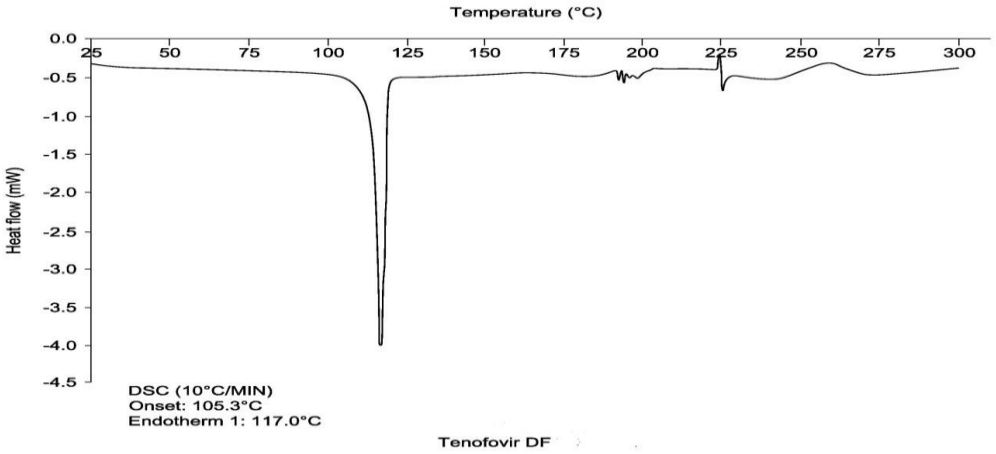


Fig 1: DSC image of Tenofovir disoproxil fumarate pure drug.

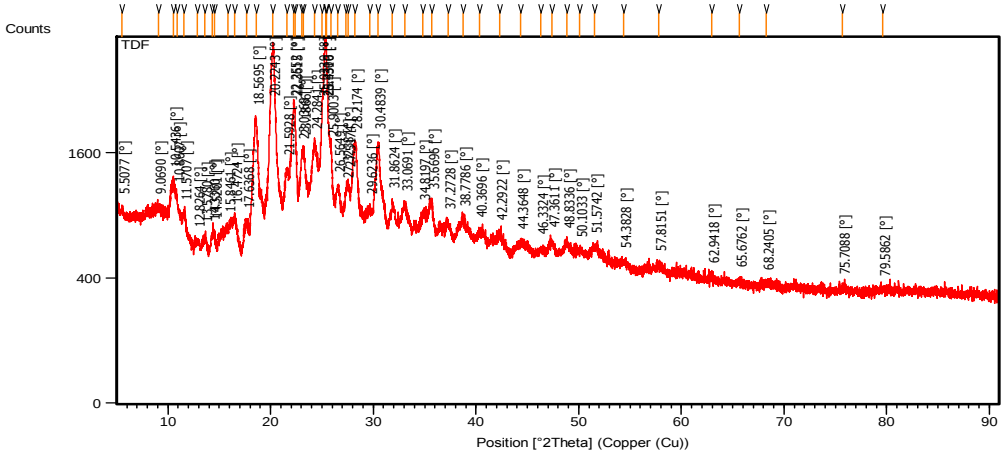


Fig 2: XRD image of Tenofovir disoproxil fumarate pure drug.

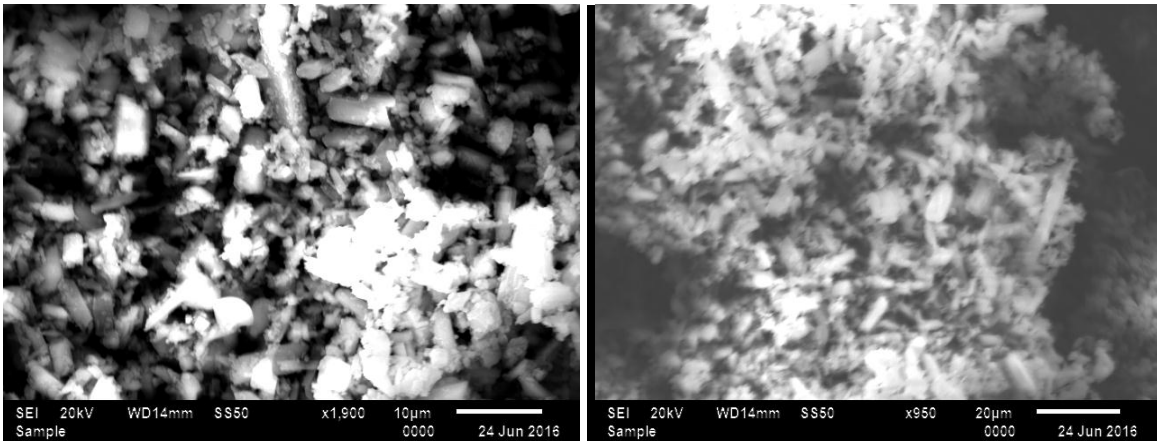
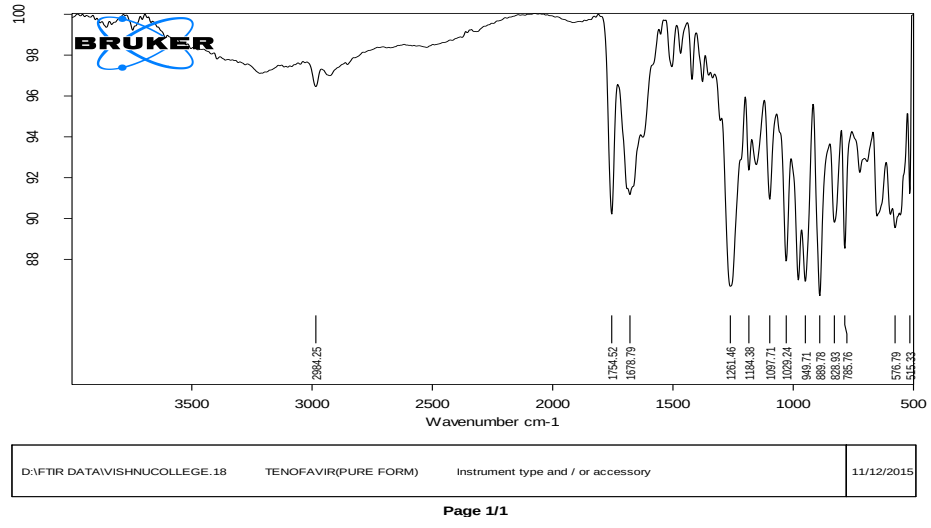
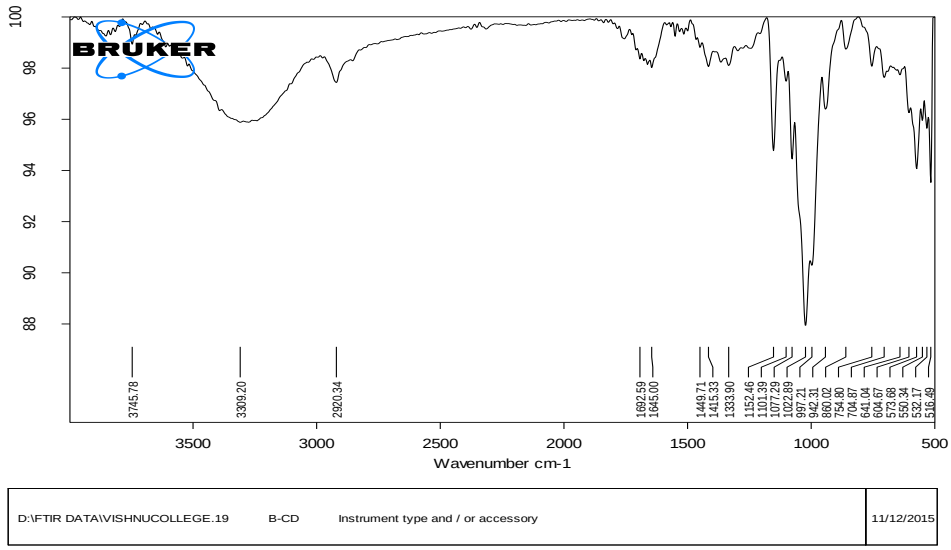


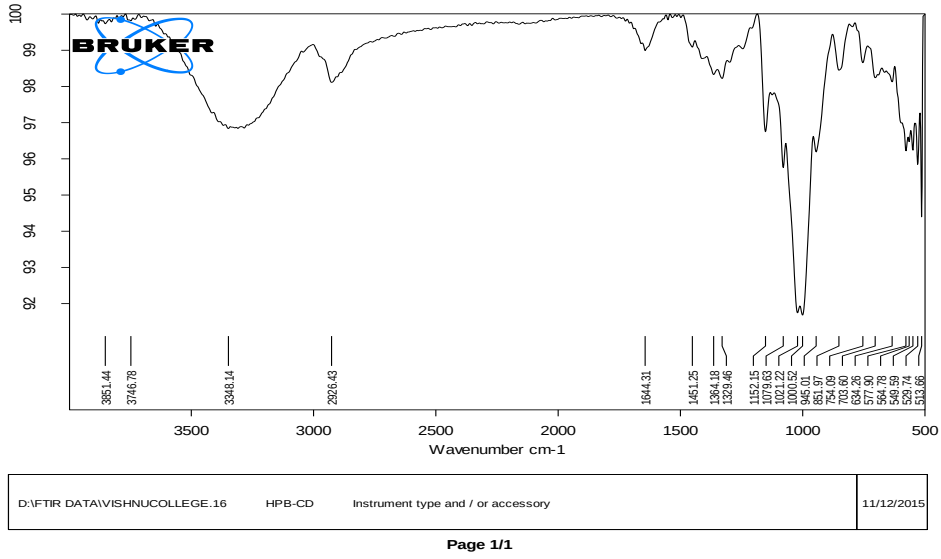
Fig 3: SEM image of Tenofovir disoproxil fumarate pure drug. Tenofovir disoproxil fumarate showed morphological structure of the particle and the diameter of the particle.



(A)



(B)



(C)

Fig 4: FTIR spectra's of (A) TDF (B) β-CD (C) HP-β-CD

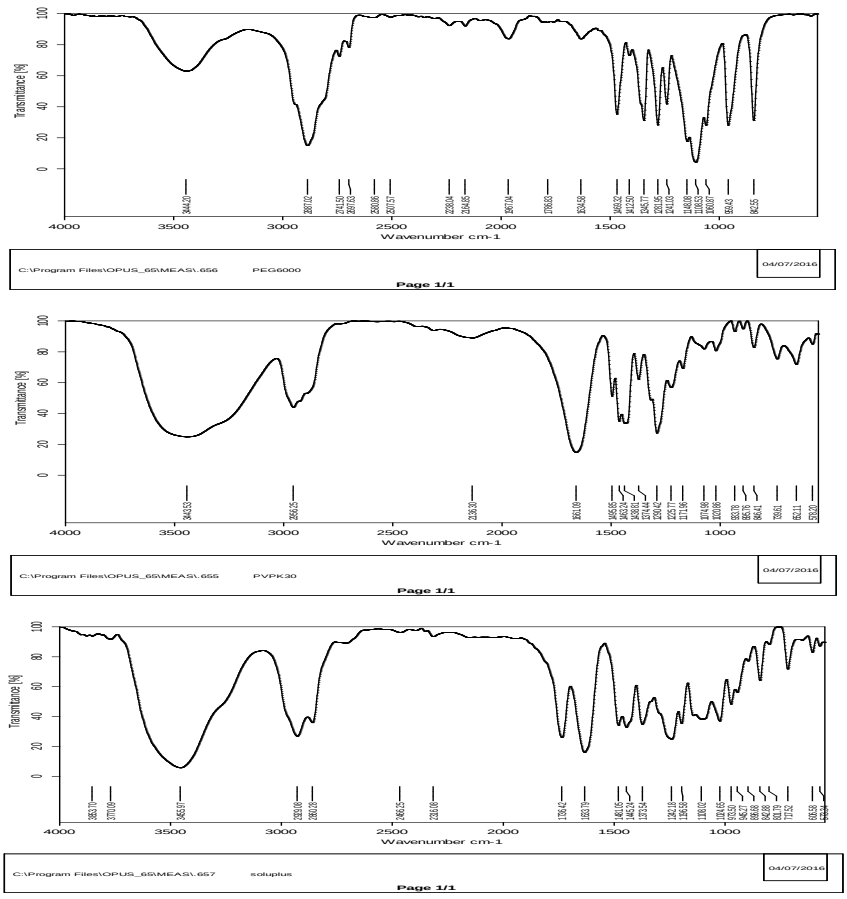


Fig 5: FTIR spectra's of (A) PEG 6000, (B) PVPK30, (C) Soluplus

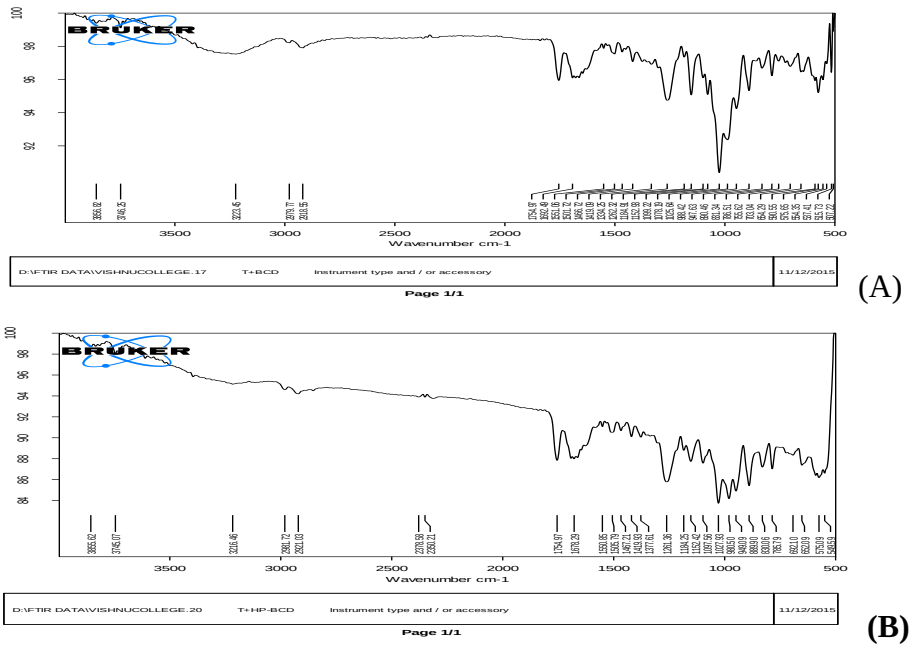


Fig 6: FTIR spectra's of (A) TDF + β-CD, (B) TDF + HP-β-CD

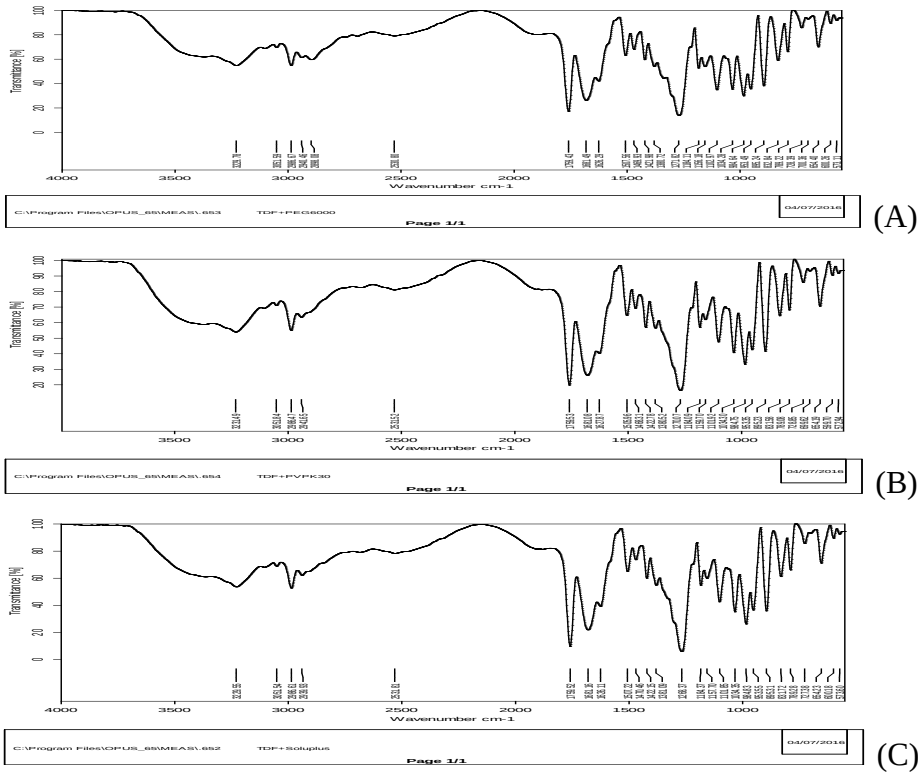


Fig 7: FTIR spectra's of (A) TDF + PEG 6000, (B) TDF + PVPK30, (C) TDF + Soluplus.

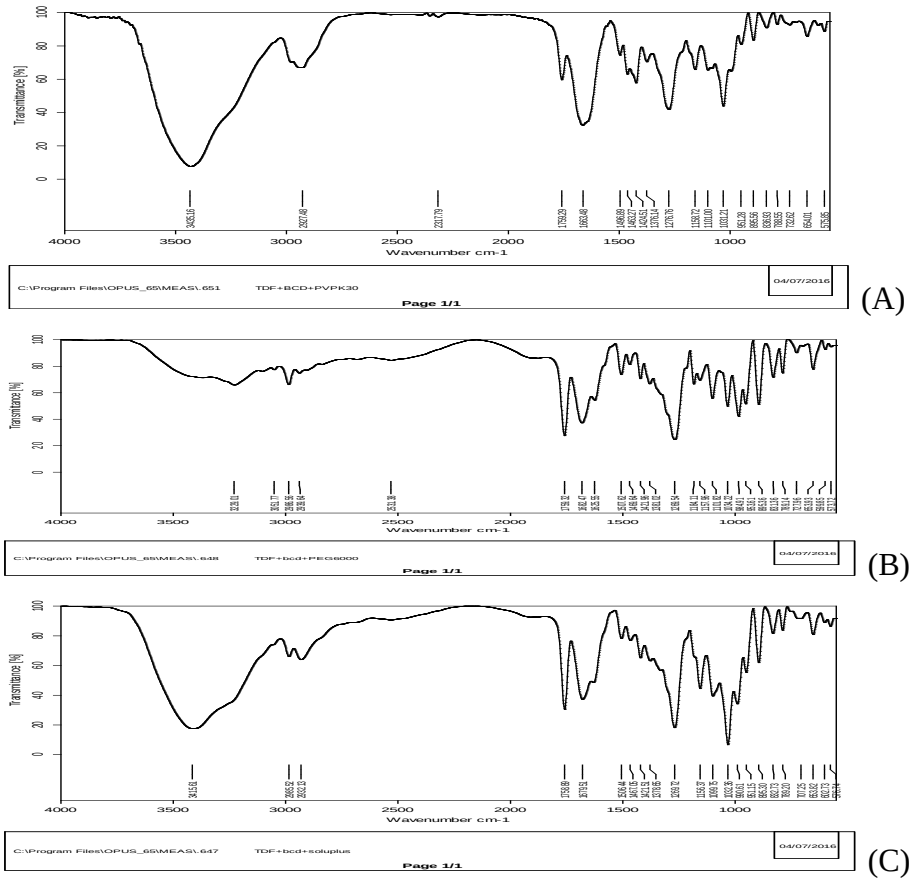


Fig 8: FTIR spectra's of (A) TDF+β-CD + PEG6000 (B) TDF + β-CD + PVPK30, (C) TDF + β-CD + Soluplus.

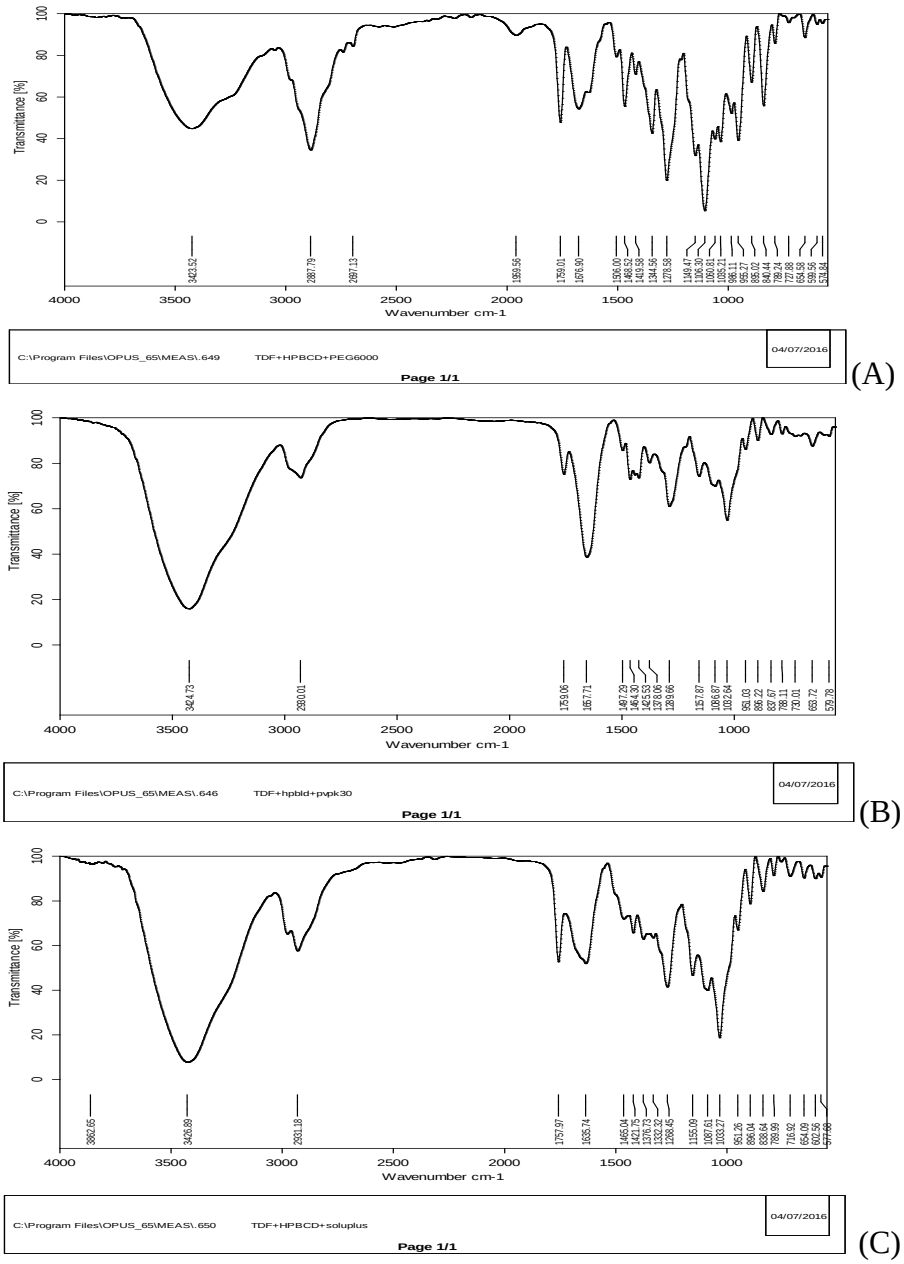


Fig 9: FT-IR spectra's of (A) TDF + HP-β-CD + PEG 6000, (B) TDF +HP-β-CD + PVPK30, (C) TDF + HP-β-CD + Soluplus.

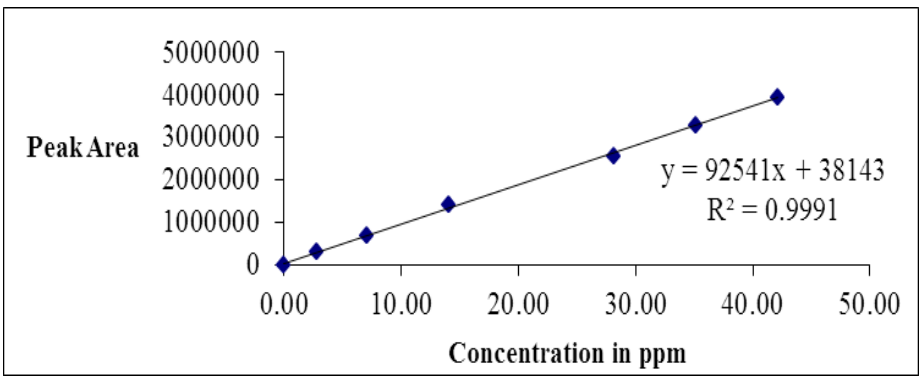
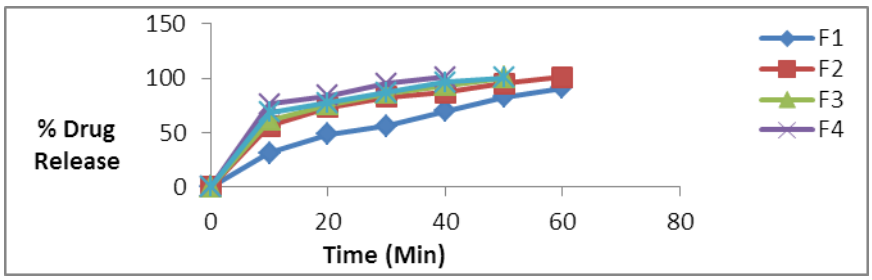


Fig 10: standard calibration curve for Tenofovir disoproxil fumarate.

I*n-vitro* studies

Table 3: *In-vitro* Dissolution profiles of Tenofovir disoproxil fumarate FDTs containing drug as inclusion complexes and super disintegrants.

% DRUG RELEASE FOR TENOFOVIR DISOPROXIL FUMARATE FDTS 0.1N HCl at 260nm									
Formulation	**10 min**	**20 min**	**30 min**	**40 min**	**50 min**	**60 min**	**DE30 (%)**	**T_{50} (min)**	**K_1 (min)**
F_1	31.66	48.51	56.32	69.62	82.49	91.15	41.55	43.31	0.0163
F_2	56.25	73.23	82.52	86.66	94.93	100.72	63.44	29.74	0.0233
F_3	61.75	75.66	86.47	93.32	100.53	------	65.36	24.83	0.0279
F_4	76.50	83.88	94.90	100.95	------	------	74.94	17.19	0.0403
F_5	68.58	77.42	86.57	96.05	100.55	------	68.52	21.72	0.0319
F_6	81.50	95.52	100.32	--------	-------	------	81.80	10.26	0.0675
F_7	59.75	68.21	76.04	95.98	100.45	------	60.17	22.94	0.0302
F_8	69.83	78.26	91.18	100.06	--------	------	70.58	21.06	0.0329
F_9	79.16	86.98	94.91	100.88	-------	------	76.59	16.98	0.0408
F_{10}	76.33	87.90	95.51	100.68	-------	------	76.59	15.96	0.0434



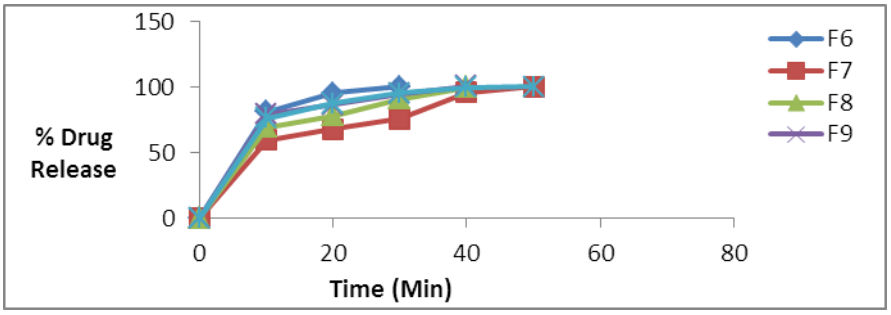
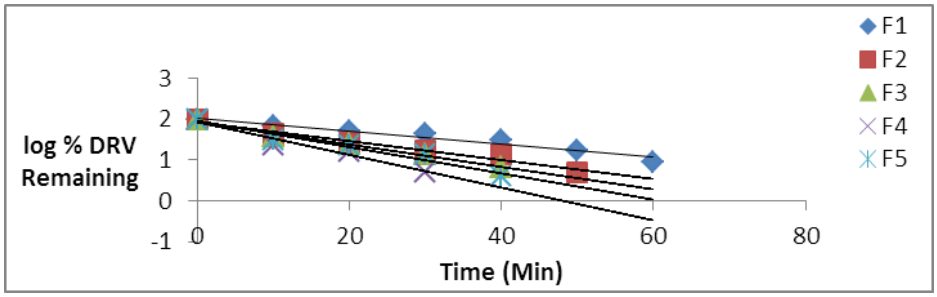


Fig 11: Dissolution Profile of Tenofovir disoproxil fumarate FDT'S Containing Drug as Inclusion Complexes and Superdisintegrants.



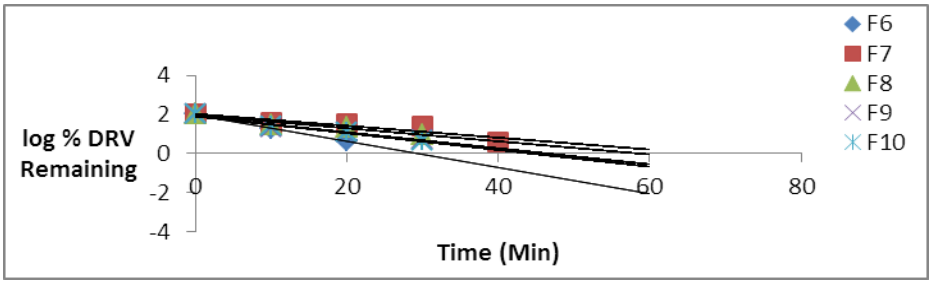


Fig 12: First order dissolution plots of Tenofovir disoproxil fumarate FDT'S Containing Drug as Inclusion Complexes and Superdisintegrants.

Table 4: Comparison of optimized (F6) Tenofovir disoproxil fumarate FDT's with control (F1) and marketed product (Tenvir).

Time (min)	Cumulative % Tenofovir disoproxil fumarate released		
	F1 (Control)	F6 (Optimized)	Tenvir (Marketed product)
0	0	0	0
10	31.66±1.23	81.50±0.3	54.16±0.2
20	48.51±0.21	95.52±0.5	69.38±0.1
30	56.32±0.55	100.32±0.4	82.00±0.1
40	69.62±0.63	---	96.36±0.4
50	82.49±0.82	---	100.49±0.2
60	91.15±0.3	---	---

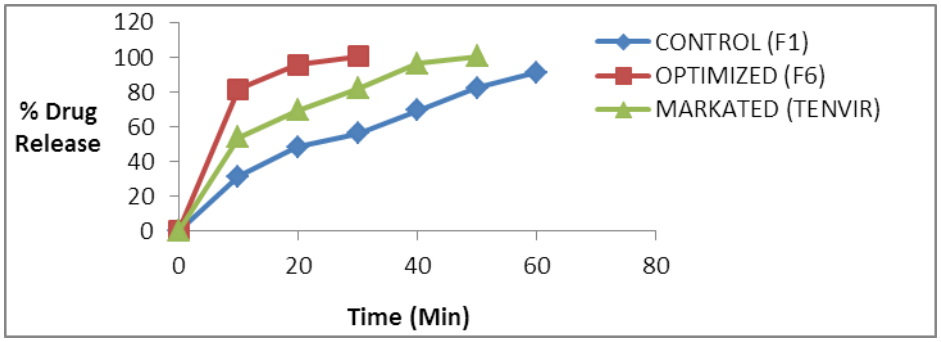


Fig 13: Comparison of dissolution profile of optimized (F6) Tenofovir disoproxil fumarate FDT's with control (F1) and marketed product, (TENVIR).

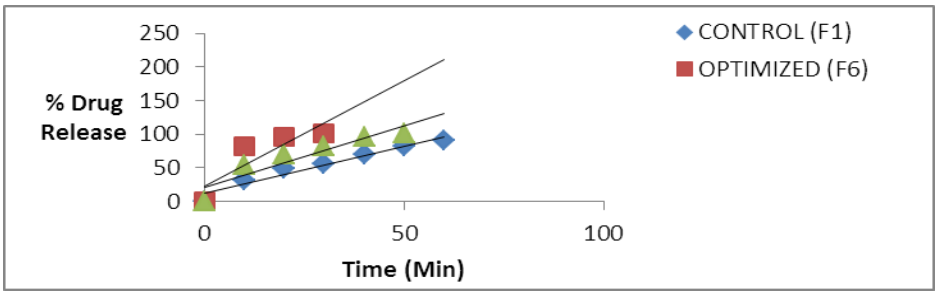


Fig 14: Comparison of the zero order plot of optimized (F6) Tenofovir disoproxil fumarate FDT's with control (F1) and marketed product, (TENVIR).

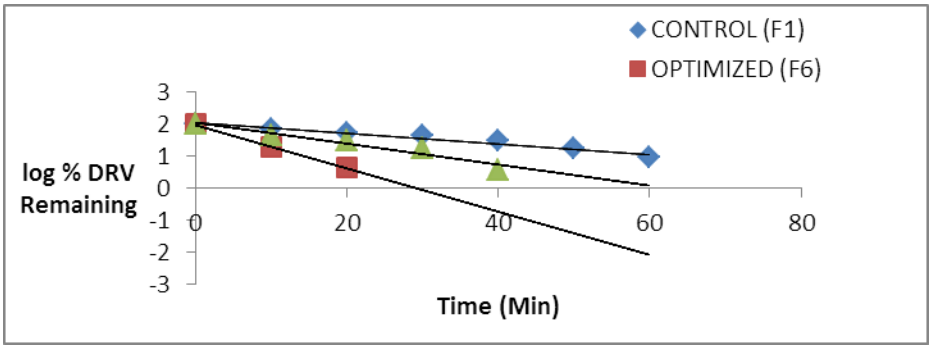


Fig 15: Comparison of first order plot of optimized (F6) Tenofovir disoproxil fumarate FDT's with control (F1) and marketed product. (TENVIR)

Table 5: Evaluation of Pre-compression Parameters of Tenofovir disoproxil fumarate granules.

Formulation	Angle of Repose (θ) *	Bulk density (gm/cm^3) *	Tapped density (gm/cm^3) *	Compressibility Index (%)*	Hausner's ratio*
F1	29.5±0.03	0.54±0.02	0.60±0.03	14.00±1.16	1.18±0.02
F2	28.6±0.00	0.53±0.01	0.64±0.02	15.00±1.32	1.14±0.04
F3	26.6±0.01	0.56±0.03	0.66±0.02	12.75±1.22	1.16±0.03
F4	25.8±0.01	0.55±0.04	0.68±0.07	13.50±0.46	1.15±0.05
F5	29.1±0.05	0.58±0.01	0.67±0.02	12.29±0.39	1.18±0.03
F6	23.2±0.01	0.59±0.04	0.65±0.04	18.11±0.55	1.18±0.07
F7	27.1±0.01	0.57±0.01	0.69±0.01	17.06±1.12	1.02±0.09
F8	28.2±0.01	0.56±0.01	0.69±0.04	19.29±0.54	1.18±0.04
F9	26.4±0.03	0.58±0.01	0.66±0.03	17.38±0.37	1.13±0.05
F10	28.2±0.02	0.59±0.01	0.67±0.02	12.12±0.51	1.11±0.06

Table 6: Evaluation of Post-compression Parameters of Tenofovir disoproxil fumarate FDTs.

Formulation	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Weight variation (%)	Drug content (%)	Disintegration Time (sec)*	Wetting Time (sec)
F1	5.4±0.03	3.2±0.01	0.52±0.02	2.1±0.33	95.27 ± 0.15	150±1.1	122 ±11
F2	5.9±0.02	3.3±0.01	0.45±0.03	2.4±0.13	96.13±0.26	56±2.2	72±12
F3	5.7±0.01	3.4±0.08	0.40±0.05	2.6±0.20	91.28±1.22	69±3.1	63±13
F4	5.5±0.04	4.2±0.33	0.41±0.04	2.2±0.54	93.16±0.18	53±1.0	52±14
F5	5.9±0.08	4.3±0.18	0.52±0.06	2.8±0.21	97.22 ±0.25	68±1.3	77±13
F6	5.7±0.06	4.2±0.37	0.53±0.01	2.2±0.33	100.21 ±0.25	26±1.3	68±17
F7	5.3±0.04	3.1±0.45	0.51±0.03	2.8±0.32	98.34 ±0.15	42±1.0	59±18
F8	5.8±0.03	3.6±0.33	0.49±0.04	2.7±0.41	99.34±0.25	35±1.3.	66±15
F9	5.5±0.02	3.7±0.23	0.53±0.04	2.3±0.30	94.28±0.19	56±1.2	56±16
F10	5.7±0.04	4.6±0.50	0.51±0.03	2.4±0.23	93.18±0.25	30±13	62±17

CONCLUSION

Tenofovir disoproxil fumarate is a drug which suffers from poor bioavailability when administered in the form of conventional tablets because of its high hydrophobicity and poor aqueous solubility. Complexation with cyclodextrins and the incorporation of hydrophilic polymers have been useful strategies in improving the solubility and dissolution characteristics of Tenofovir disoproxil fumarate. The basic method considered for the development of Tenofovir disoproxil fumarate fast dissolving tablets is the direct compression method by using Mannitol as diluent and CCS, CPV and SSG, as super disintegrating agents at different concentrations (10, 20 and 30%) with the drug in a ternary complex form, D: HP-β-CD: Soluplus (1:0.5:0.50). Based on the disintegration time and wetting time, super disintegrants can be ranked as Croscarmellose sodium (CCS) > Crospovidone (CPV) > Sodium starch glycolate (SSG). From the *in-vitro* dissolution studies, the optimum concentration of super disintegrants, Croscarmellose sodium (CCS) was found to be 20% w/w in the disintegration time and wetting time, Formulation with CPV showed lesser degrees of weight variation, and % friability loss and better hardness when compared to other formulations. Formulations containing 20% of CSS (F6) rapidly disintegrated and fulfilled all official requirements of FDTs. Further, the optimized formulation (F6) was compared with marketed formulation Tenvir was found to be superior in terms of dissolution profile. There was no significant variation in the physicochemical parameters, *in-vitro* disintegration time, and *in- vitro* dissolution profiles.

ACKNOWLEDGEMENT

The authors are thankful to Tenofovir disoproxil fumarate gift sample from Hetero drugs, Hyderabad. India.

REFERENCES

1. Van Schaick EA, Lechat P, Remmerie BM, Ko G, Lasseter KC, Minaret E. Pharmacokinetic comparison of fast-disintegrating and conventional tablet formulations of risperidone in healthy volunteer. Clin. Ther, 2003; 25(16): 87-99.
2. Watanabe Y, Koizumi K, Zama Y, Kiriyama M, Matsumoto Y and Matsumoto M. New compressed tablet rapidly disintegrating in saliva in the mouth using crystalline cellulose and a Disintegrants. Biol. Pharm. Bull, 1995; 18: 1308-1310.

3. Koizumi K, Watanabe Y, Morita K, Utoguchi N and Matsumoto M. New method of preparing high-porosity rapidly saliva soluble compressed tablets using mannitol with camphor, a subliming material; Int J Pharm, 1997; 152: 127-131.
4. Varley P, Yearwood R and Zydis J. A novel, fast dissolving dosage form.Manufacturing Chemist, 1990; 36: 36-37.
5. Ishikawa T, Wanatabe Y, Utoguchi Nand Matsumoto M. Preparation and evaluation of tablets rapidly disintegrating in saliva containing bitter taste masked granules by the compression method. Chem Pharm. Bull, 1997; 47(10): 1451-1454.
6. Rajyaguru T H, Indurwade N H, and Nahkhat P D. Novel approach-fast dissolving tablets. Indian Drugs, 2002; 39(8): 405-409.
7. Nadendla R R, Sudhakar G, and Srinath N. Current status of dispersible dosage forms. Int J Pharma. Excip, 2002; 2: 25-28.
8. Habib W, Khankari R, and Hontz J; Fast-dissolving drug delivery systems, critical review in therapeutics. Drug Carrier Systems, 2000; 17(1): 61-72.
9. Chang R, Guo X, Burnside B A, and Couch R. Fast-dissolving tablets; Pharm. Tech, 2000; 24(6): 52-58.
10. Dobetti L. Fast-Melting Tablets: Developments and Technologies. Pharm. Tech, 2001; 44-50.
11. Corveleyn S and Ramon J P. Formulation and production of rapidly disintegrating tablets by Lyophilization using hydrochlorothiazide as a model drug. Int J Pharm, 1997; 152: 215-225.
12. Ramon JP and Corveleyn S. Freeze-dried rapidly disintegrating tablets.US Patent, 2000; 6: 10-19.
13. Heinemann H and Rothe W. Preparation of porous tablets. US Patent, 1975; 3: 885.