INTERNATIONAL JOURNAL OF PHARMACY AND ANALYTICAL RESEARCH

ISSN: 2320-2831

IJPAR |Vol.11 | Issue 2 | Apr - Jun -2022

Journal Home page: www.ijpar.com

Research article *Open Access*

Formulation and evaluation of nevirapine extended release tablets

S.Chandra, N.Senthilkumar, S.Sundaramoorthy*, P.Divyabharathi, S.Kavibharathi, S.Sangeetha.

Department Of Pharmaceutics, JKKMMRF'S Annai JKK sampoorani ammal college of pharmacy, Ethirmedu, Komarapalayam-638183, Namakkal(DT), Tamilnadu, India

Corresponding Author: S.Chandra

ABSTRACT

Nevirapine is a non-nucleoside reverse transcriptase inhibitor (NNRTI) drug which is used in thetreatment human immunodeficiency virus type 1 (HIV-1) infections. The present study is to develop a pharmaceutically stable, cost effective, pharmaceutically equivalent, and quality improved formulation of Nevirapine ER tablets. To achieve this goal various prototype formulation trials will be taken and evaluated with respect to the various quality control tests such as dissolution, assay, acid resistance. The formula will be finalized by comparing the invitro dissolution profile with that of the marketed VIRAMUNE XR Tablets. In this study Nevirapine Extended release tablets were prepared by using hydrophobic polymers. Thirteen formulations of extended release tablets of Nevirapine were developed by using Lactose Monohydrate and Micro crystalline cellulose as diluent and Magnesium stearate aslubricant in different proportions and varying grades of Eudragit, Ethyl Cellulose and povidonein different proportions. The formulation F12 was found to be best of all the formulations showing drug release matching the innovator product. The formulation F12 was evaluated for all the quality control tests.

Keywords: Nevirapine, extended release, hydrophobic polymers, Eudragit, Ethyl cellulose.

INTRODUCTION

An ideal drug delivery system provides treatment for acute diseases or chronic illness to the patients for many years a number of oral dosage forms are available. Some are liquids (e.g: syrups, elixirs, tinctures, suspensions and emulsions), whereas the most common ones are solids (e.g: tablets and capsules). Tablets and capsules are generally formulated to release the drug immediately after oral administration to hasten systemic absorption. These are called as Immediate-release products. [1]

However, after absorption of the drug from the dosage form is complete, plasma drug concentrations decline according to the drug's pharmacokinetic profile.

Eventually, plasma drug concentrations fall below the minimum effective plasma concentration (MEC), resulting in loss of therapeutic activity. Before this point is reached, another dose is usually given if a sustained therapeutic effect is desired. An alternative to administering another dose is to use a dosage form that will provide sustained drug release, and therefore maintain plasma drug concentrations, beyond what is typically seen using immediate-release dosage forms.

The term modified-release drug product is used to describe products that alter the timing and/or the rate of release of the drug substance. A modified-release dosage form is defined "as one for which the drug-release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives. Several types of modified- release drug products are recognized. [2]

The present study is to develop a pharmaceutically stable, costeffective, pharmaceutically equivalent, and quality improved formulation of Nevirapine ER tablets. To achieve this goal various prototype formulation trials will be taken and evaluated with respect to the various quality control tests such as dissolution, assay, acid resistance. The formula will be finalized by comparing the invitro dissolution profile with that ofthe marketed VIRAMUNE XR Tablets.

MATERIALS AND METHODS

Table 1: List of the materials used in this study

S.NO	MATERIAL	Specification	MANUFACTURER
1.	Nevirapine	USP	HETERO GRUGS
2.	Lactosemonohydrate (pharmatose)	USP	ROUQUETTE
3.	MCC (avicel PH102)	USP	FMC BIOPOLYMER
4.	Eudragit RS 30 D	USP	EVONIK INDUSTRIES
5.	Eudragit RSPO	USP	EVONIK INDUSTRIES
6.	Ethocel std 10 premium EC	USP	COLORCON ASIA PVT.LTD
7.	Ethocel std 45 premium EC	USP	COLORCON ASIA PVT.LTD
8.	Magnesium stearate	USP	FERRO INDUSTRIES
9.	Sodium steryl fumerate	USP	FERRO INDUSTRIES

Preformulation Study [3]

Preformulation study is an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. It is the first step in the rationale development of dosage form.

Formulation Development

Based on preformulation data the various excipients were selected and their compilation isshown in the below table.

Table 2: Composition of Nevirapine ER tablets F1 to F5

S.No	INGREDIENTS	mg/tablet				
		F1	F2	F3	F4	F5
DRY MIX						
1.	Nevirapine	400	400	400	400	400
2.	Lactose monohydrate	407.5	420	420	430	440
3.	MCC (Avicel PH 102)	122.5	140	140	140	140
BINDER SOLUTION						
4.	Plasdone K 90 D	_	_	_	_	_
5.	Eudragit RS 30 D	_	_	_	_	_
6.	Eudragit RSPO	_	_	_	_	_
7.	Ethocel std 10 premium EC	60	30	_	_	_
8.	Ethocel std 45 premium EC	_	_	30	20	10
9.	Water	_	_	_	_	_
10.	IPA	Qs	Qs	Qs	Qs	Qs
LUBRICATION						
11.	Magnesium Stearate	10	10	10	10	10

12.	Sodium steryl fumarate	_	_	_	_	_

Table 3: Composition of Nevirapine ER tablets F6 to F9

S.No	INGREDIENTS	mg/tablet			
		F6	F7	F8	F9
	DRY MIX				
1.	Nevirapine	400	400	400	400
2.	Lactose monohydrate	407	350	260	140
3.	MCC (Avicel PH 102)	133	140	140	260
	BINDER SOLUTION				
4.	Plasdone K 90 D	_	_	_	_
5.	Eudragit RS 30 D	50	50	80	80
6.	Eudragit RSPO	_	50	110	110
7.	Ethocel std 10 premium EC	_	_	_	_
8.	Ethocel std 45 premium EC	_	_	_	_
9.	Water	Qs	Qs	Qs	Qs
10.	IPA	_	_	_	_
	LUBRICATION				
11.	Magnesium Stearate	10	_	_	_
12.	Sodium steryl fumarate	_	10	10	10

Table 4: Composition of Nevirapine ER tablets F10 to F13

S.No	INGREDIENTS	mg/tablet			
		F10	F11	F12	F13
DRY MIX					
1.	Nevirapine	400	400	**400**	400
2.	Lactose monohydrate	400	400	**400**	400
3.	MCC (Avicel PH 102)	140	150	**156**	158
BINDER SOLUTION					
4.	Plasdone K 90 D	50	40	**44**	42
5.	Eudragit RS 30 D	_	_	_	_
6.	Eudragit RSPO	_	_	_	_
7.	Ethocel std 10 premium EC	_	_	_	_
8.	Ethocel std 45 premium EC	_	_	_	_
9.	Water	Qs	Qs	Qs	Qs
10.	IPA	_	_	_	_
LUBRICATION					
11.	Magnesium Stearate	10	10	**10**	10
12.	Sodium steryl fumarate	_	_	_	_

Nevirapine ER tablets

Nevirapine anhydrous is fluffy and poorly flowable material. So, for formulation of Nevirapine extended release tablets direct compression approach is not pursued and trails were initiated by wet granulation approach with varying concentrations of polymer proportions using Ethylcellulose, Eudragit, Povidone.

Manufacturing forcess of nevirapine er tablets

Sifting: NVP anhydrous, MCC and Lactose monohydrate are sifted through 30# mesh.

Dry mixing: Sifted material of step 1 were transferred into rapid mixer granulator and mixed for 10min with impeller at slow speed and chopper off.

Preparation of binder solution: Required quantity of purified water is taken in a stainless steel container equipped with a propeller stirrer. Binder was added slowly to purified water while stirring**,** speed of stirrer

is increased ifnecessary. Stirring is continued for 10min or till clear solution is obtained.

Wet granulation: Dry mix of step 2 is granulated by adding binder solution of step3.2 over a period of 2min with impeller at slow speed and chopper off and the amperage recording of the impeller motor was recorded. Based on granulation consistency additional quantity of purified water is added if requiredover a period of 1min impeller at slow speed. The impeller and inner walls of the bowl is scraped using scraper or spatula. Mixing is continued for 1-2min with impeller and chopper at slow speed. Complete formation of granulesis checked. Wet granules are discharged while mixing impeller at slow speed.

Drying: Wet mass is loaded into FBD and air dried for 5min to ensure proper fluidization. The wet mass is dried with inlet temperature of 60 ± 5^0c till loss on drying is NMT 2%m/m is achieved when determined using moisture analyzer in auto mode at 105^0c.

Sifting and milling: Granules of step 5.2 are sifted through mesh#20. Retentions of the sieve #20 ASTM are collected. Retained granules of step 6.1 are milled using multi mill fitted with 1.gmm screen at medium speed and knives forward direction. Material of step 6.2 are sifted through sieve#20 ASTM, over granules (retained over sieve)are present, step 6.2 and 6.1 are repeated till all the oversize granules pass through sieve #20 ASTM.

Sifting: Sift Magnesium stearate through mesh#60.

Lubrication: The sifted material of step 6.3 and step 7.1 are loaded into octagonal blender and mixed for5min.

Compression: Tooling: 19.20 x 9.30mm, oval shape, standard concave embossed with 'H' on upper punch and'N1' on lower punch.

Table 5: Compression parameters

S.No	Parameter	Specification
1.	Tablet description	White to off-white, oval, biconvex tablets debossed with 'H' one side and 'N1' on other side
2.	Individual weight variation	1000±2% (980.00-1020.00mg)
3.	Weight variation of 10 tablets(gm)	10.000gm ±3% (9.7-10.3gm)
4.	Hardness (kps)	17-19
5.	Thickness (mm)	7±3mm
6.	Friability(%w/w)	NMT 1%

Evaluation of NEVIRAPINE extended release tablets

All the prepared tablets were evaluated for the following parameters as per the guidelines and the results are given in the Table.

The present study was undertaken to formulate Nevirapine extended release tablets. The study involves preformulation studies of drug and excipients, formulation and processing development along with evaluation of tablets made with the optimized formulation. Finally extended release tablets were evaluated by in vitro methods.

RESULTS

Table 6: Preformulation studies

S.No.	Characteristics	Results
1.	Organoleptic Evaluation	White to off-white colored crystalline powder.
2.	Solubility Analysis	Practically insoluble in water, sparingly soluble in methylenechloride, slightly soluble in methanol, soluble in chloroform.
3.	Bulk density	0.289g/ml
4.	Tap density	0.458g/ml
5.	Compressibility index	36.89%
6.	Hausner's ratio	1.58

7.	Melting point	196.06^{0}C

Drug – Excipients compatibility studies

Physical observation of sample was done every week for any colorchange or lumps formation and flow, the results of the physical observation were shown in table.

Table 7: drug excepient compatibility study results

S.No	Name of the excipient	Drug/ Excipient ratio	Category	Composition (each gram of blend contains)	Observations			
					Storage condition/ Duration			
					400c/75%RH			
					Initial	1M	2M	3M
1.	Nevirapine alone	_	API		NCC	NCC	NCC	NCC
2.	Nevirapine + Lactose Monohydrate (Pharmatose 200M)	1:2	Filler	0.34 gm of nevirapine and 0.68 gm pharmatose 200M	NCC	NCC	NCC	NCC
3.	Nevirapine + Microcrystalline cellulose (pH 102)	1:2	Filler	0.34 gm of nevirapine and 0.68 gm of Microcrystalline cellulose pH 102	NCC	NCC	NCC	NCC
4.	Nevirapine + Ethyl cellulose (ethocel std premium EC)	1:0.25	Binder	0.8 gm of nevirapine and 0.2 gm Ethocel std 10 premium EC	NCC	NCC	NCC	NCC
5.	Nevirapine + Ethyl cellulose (ethocel std 45 premium EC)	1:0.25	Binder	0.8 gm of nevirapine and 0.2 gm of ethocel std 45 premium EC	NCC	NCC	NCC	NCC
6.	Nevirapine + Eudragit RS 3D	1:0.25	Binder	0.8 gm Nevirapine and 0.2 gm of Eudragit RS 3D	NCC	NCC	NCC	NCC
7.	Nevirapine + Eudragit RSPO	1:0.25	Binder	0.8 gm ofnevirapine and 0.2 gm of Eudragit RSPO	NCC	NCC	NCC	NCC
8.	Nevirapine + Povidone (plasdone K 90)	1:0.25	Binder	0.8 gm ofnevirapine and 0.2 gm of Plasdone K 90	NCC	NCC	NCC	NCC
9.	Nevirapine + Magnesium stearate	1:0.25	Lubricant	0.95 gm ofnevirapine and 0.047 gm Of agnesium stearate	NCC	NCC	NCC	NCC
10.	Nevirapine + Sodium stearylfumerate	1:0.25	Lubricant	0.95 gm ofnevirapine and 0.047 gm ofSodium stearyl Fumerate	NCC	NCC	NCC	NCC

Table 8: Chemical characterization of API for Development

S.No	Test	Specifications	Results
1.	Description	A white to off-white crystalline powder	An white crystalline powder
2	Solubility	Practically insoluble in water, slightly soluble in alcohol, methanol.	Complies
3.	Identification by infrared absorption	Similar to standard	Complies
4.	Water content	Not more than 0.2% m/m	Complies

5.	Residue on ignition	Not more than 0.1%m/m	0.04% m/m
6.	Heavy metals	Not more than 0.001%m/m	0.03% m/m
7.	Chromatographic purity by HPLC	Nevirapine related compound – A not morethan 0.15% m/m	0.02%m/m
		Nevirapine related compound – B not morethan 0.15% m/m	0.02%m/m
		Nevirapine related compound – C not morethan 0.10% m/m	Below LOQ
		Nevirapine Impurity : not more than 0.10%	Below LOQ
		Maximum single unknown impurity: notmore than 0.105m/m	0.01% m/m
		Total impurities: NMT 0.60%m/m	99.1% m/m
8.	Assay by UV	Between 98.0% and 101.0% m/m	99.1%
9.	Residual solvents byGC	Methylene chloride: not more than 600 ppm	215 ppm
		Chloroform : not more than 60 ppm	16 ppm
		O-Xylene : not more than 190 ppm	7 ppm

FTIR studies

IR spectra was obtained by using the FTIR spectrophotometer (H400-84100, Shimadzu, Japan) using KBR pellets and scanning range was 4400 to 400 cm^{-1} at a scan period of 1 min. The FTIR spectra of pure drug, drug with excipients and only excipients are shown in figure 1-3. From this it is clear that the characteristic peaks at 3432.82 (C=O stretching), 1645.90 (C=N stretching), 1548.76 (NH stretching) and the NH bond in plane (1463.69) shows the presence of the drug are present in both the pure drug, formulation without any change in their positions, indicating no chemical interaction between drug and excipients, as confirmed by the FTIR studies.

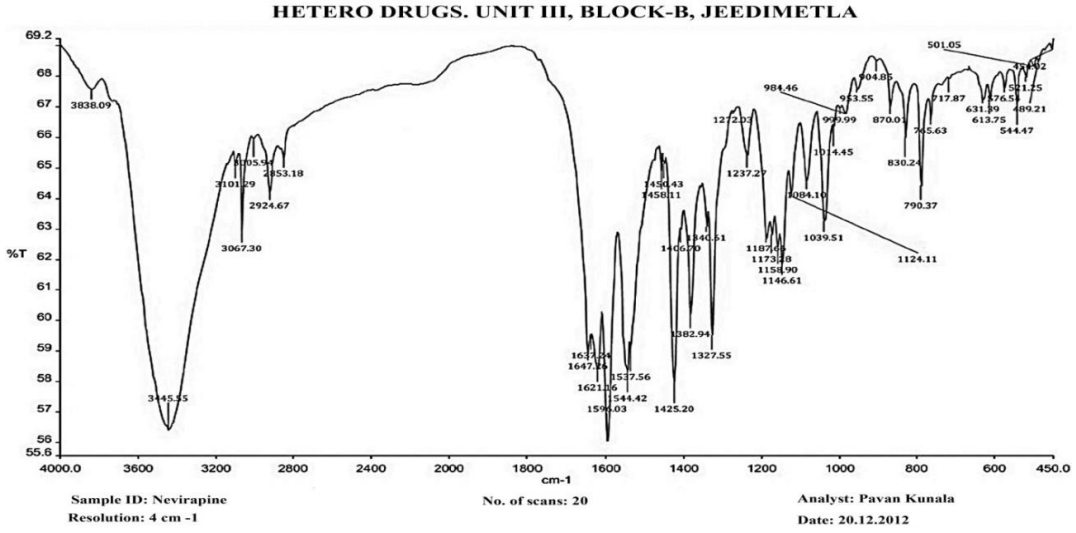

Fig 1: FTIR spectral obtained for pure drug

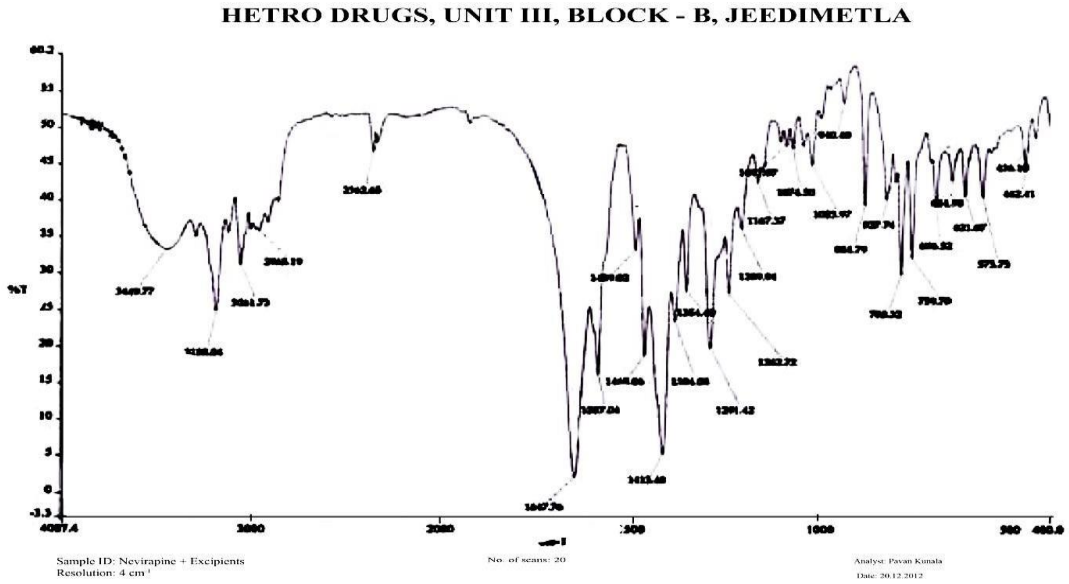

Fig 2: FTIR spectra obtained for Nevirapine along with excepients

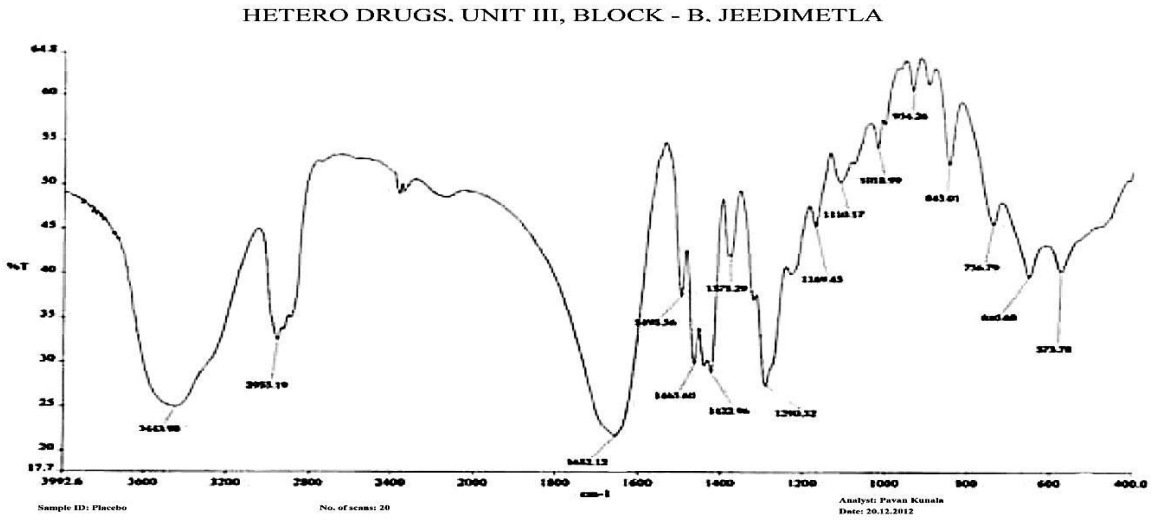

Fig 3: FTIR spectra obtained for Nevirapine Excipients

There is no change in the shape of the peak or shift of the peak hence there was no chemicalinteraction between drug and excipients as confirmed by FTIR studies.

EVALUATION OF FORMULATIONS

Physical Evaluation

Table 9: Physical Evaluation of formulation 1 to 6

S. No	Physical parameter	F1	F2	F3	F4	F5	F6
1.	Weight variation (±5%)	1.44	1.38	1.63	1.23	1.42	1.57
2.	Hardness(kp)	15.6	16	15.3	18	16.4	15.3
3.	Friability	0.17	0.19	0.21	0.10	0.19	0.18
4.	Thickness	7.0	6.8	6.8	7.1	7.1	7.2

Table 10: Physical Evaluation of formulation 7 to 13

S.No	Physical parameter	F7	F8	F9	F10	F11	F12	F13
1.	Weight variation (±5%)	1.54	1.35	1.28	1.44	1.57	1.65	1.18
2.	Hardness(kp)	16	15.3	16	18.7	17	18.2	19
3.	Friability	0.19	0.2	0.22	0.18	0.2	0.12	0.17
4.	Thickness	7.3	7.0	7.0	7.4	6.9	6.9	7.0

Chemical Evaluation

Table 11: Chemical Evaluation of formulation 1 to 6

S. No	Parameters	F 1	F 2	F 3	F 4	F 5	F 6
1.	Assay (90-110%)	100.2	99.6	98.9	98.3	101.2	98.0

Table 12: Chemical Evaluation of formulation 7 to 13

S. No	Parameters	F 7	F 8	F 9	F 10	F 11	F 12	F 13
1.	Assay (90-110%)	101.2	99.8	98.2	98.2	98.4	99.6	99.4

DISSOLUTION STUDIES

The dissolution was carried out for different experimental trials and also for the innovator. The various results that are obtained are tabulated below. Dissolution studies are carried out in the following media.

Buffer Stage: (pH 6.8)

Apparatus :USP Type I (Basket 10mesh size)
Dissolution medium : 2% SLS in pH 6.8 phosphate bufer.
Volume : 900 ml
RPM : 100
Temperature : 37 ± 0.5°C
Time : 2, 4, 8, 12, 14, 18, and 24 hours.

Table 13: Dissolution Profile of Viramune XR (innovator)

	% Drug dissolved in time (hrs)							
Unit	**0**	**2 (NMT-30%)**	**4**	**8 (50-80%)**	**12**	**14**	**18 (NLT-80%)**	**24**
1	0	19	36	62	83	93	96	98
2	0	20	37	66	88	94	97	99
3	0	19	36	67	89	94	95	98
4	0	20	40	68	88	95	97	99
5	0	20	38	68	89	96	97	98
6	0	19	36	65	87	95	97	98
Average	0	19	37	66	87	94	97	98
%RSD	0	1	2	2	2	1	1	1

Table 14: Drug Release Kinetics

Batch	Zero order	First order	Higuchi	Korsmeyer-Peppas		f_1 value	f_2 value
	r^2	r^2	r^2	r^2	n	-	-
INNOVATOR	**0.8417**	**0.9706**	**0.9489**	**0.9476**	**0.6942**	-	-

F1	0.9386	0.9796	0.9498	0.9309	0.9608	40	27
F2	0.9423	0.9803	0.9937	0.774	0.5495	27	35
F3	0.8992	0.9761	0.9967	0.723	0.5008	48	15
F4	0.9118	0.7665	0.9216	0.7533	0.551	34	21
F5	0.9006	0.9904	0.9801	0.8109	0.670	15	47
F6	0.9206	0.7796	0.9827	0.7459	0.5609	47	15
F7	0.9393	0.8231	0.989	0.7794	0.617	27	23
F8	0.9247	0.9307	0.9162	0.9518	1.0645	28	23
F9	0.933	0.9741	0.9607	0.8847	0,8089	33	31
F10	0.9638	0.9469	0.8788	0.9194	0.678	79	12
F11	0.7056	0.8623	0.9099	0.6257	0.2586	57	14
F12	0.8283	**0.9797**	0.9553	0.9532	**0.5996**	3	79
F13	0.966	0.9174	0.9838	0.7815	0.6406	44	16

*** r^2 = Correlation coefficient, n= Diffusional exponent.**

RELEASE MECHANISM

Based on the "n" value of 0.599 obtained for F12 formulation, the drug release was found to follow Anomalous (non-Fickian) diffusion[4]. This value indicates a coupling of the diffusion and erosion mechanism (Anomalous diffusion) and indicates that the drug release was controlledby more than one process. Based on the value of "n" (n=0.694) for innovator product, it was alsofound to follow the same release mechanism.

Also, the drug release mechanism was best explained by first order equation, as the plots showedthe highest linearity (r^2 = 0.9797), followed by Higuchi's equation (r^2 = 0.9553). As the drug release was best fitted in first order kinetics, it indicated that the rate of drug release is concentration dependent. Even the innovators product was found to follow the same pattern with the highest linearity (r^2 = 0.9706) for the first order equation. [5]

The "r" value for Higuchi plot was found to be 0.9489 indicating that the drug release included diffusion as one of the release mechanisms.

The dissolution profiles of formulation F12 and innovator product were compared by calculating differential factor (f1) and similarity factor (f2). The f1 and f2 were found to be 3.0% and 79.0%respectively for the comparison of dissolution profiles of formulation F12 and innovator product.Hence these two products were considered to be similar.

SIMILARITY FACTOR AND DISSIMILARITY FACTOR CALCULATION [6]

The similarity factor (f_2) was defined by CDER, FDA, and EMEA as the "logarithmic reciprocal square root transformation of one plus the mean squared difference in percent dissolved between the test and reference release profiles".

Dissimilarity or difference factor (f_1) describes the relative error between two dissolution profiles. It approximates the percent error between the curves. The percent error is zero when thetest and reference release profiles are identical and increases proportionally with the dissimilaritybetween the two profiles.

There are several methods for dissolution profile comparison. The f_2 is the simplest among those methods. Moore & Flanner proposed a model independent mathematical approach to compare the dissolution profile using the two factors f_1 & f_2.

$$f_1 = \{ [\sum_{t=1}^{n} |R_t - T_t|] / [\sum_{t=1}^{n} R_t] \} . 100$$

$$f_2 = 50. Log \{ [1 + (1/n) \sum_{t=1}^{n} (R_t - T_t)^2]^{-0.5} . 100\}$$

Where 'R_t' and 'T_t' are the cumulative percentage drug dissolved at each of the selected n time point of the reference & test product respectively. The factor f_1 is proportional to the average difference between the two profiles, where as factor f_2 is inversely proportional to the averaged squared difference between the two profiles, with emphasis on the larger difference among allthe time points. The similarity factor f_2 and its significance is shown in the following table

Table 15: Similarity factor f2 and its significance [7]

S. No.	Similarity factor (f2)	Significance
1.	<50%	Test and reference profiles are dissimilar.
2.	50 -100%	Test and reference profiles are similar.
3.	100%	Test and reference profiles are identical.
4.	>100%	The equation yields a negative value.

Table 16: f_2 value calculation

DISSOLUTION PROFILE COMPARISION						
Time (hrs)	**INNOVATOR(R)**	**F13 (T)**	**(R-T)**	**$(R-T)^2$**	**|R-T|**	**f_2 value**
0	0	0	0	0	-	
2	19	24	5	25	**1.6**	
4	37	41	4	16	**1.3**	
8	66	68	2	4	**0.69**	**79.0%**
12	87	88	1	1	**0**	
14	94	94	0	0	-	
18	97	96	1	1	**0**	
24	98	98	0	0	-	
TOTAL	**498**	**509**	**13**	**169**	**3.58**	

Since the f_2 value of formulation 13 is 79.0%, the formulation is said to be similar to that of thereference product of Viramune XR tablets.

STABILITY STUDIES [8,9]

Table 17: Stability Data for F 12

Batch number and stability condition	Tablet Description	Water by KF	Assay (%)	Drug Release in pH 6.8 buffer after 24hrs
Room temperature (Initial)	White oval shaped tablet debossed with 'H' on one side and 'N1' on other side.	0.04%	100.4%	98
40°C /75%RH (1month)	White oval shaped tablet debossed with 'H' on one side and 'N1' on other side.	0.04%	100.4%	98
40°C/75% RH (2months)	White oval shaped tablet debossed with 'H' on one side and 'N1' on other side.	0.04%	99.6%	98
40°C/75% RH (3months)	White oval shaped tablet debossed with 'H' on one side and 'N1' on other side.	0.04%	99%	98
25°C/60% RH (1month)	White oval shaped tablet debossed with 'H' on one side and 'N1' on other side.	0.04%	100%	98
25°C/60% RH (2months)	White oval shaped tablet debossed with 'H' on one side and 'N1' on other side.	0.04%	99.6%	98
25°C/60% RH (3months)	White oval shaped tablet debossed with 'H' on one side and 'N1' on other side.	0.04%	99.6%	98

DISCUSSION

The objective of the study is to formulate and evaluate Nevirapine Extended Release tablets and to compare with the innovator product. Extended-release antiretroviral (Nevirapine) drug formulation can help achieve the primary treatment goals for many patients with HIV preventing or reducing side effects. The dosing flexibility and consistency of serum levels conferred by extended-release formulations help achieve these goals.During the drug-excipient interaction study it was observed that there was no significant physicalchange in the drug when mixed with excipients and kept under stressed conditions for three months.

To fix a target release profile, *in-vitro* release study

of the innovator's product (Viramune XR by BoehringerIngelheim Ltd.) was carried out. Based on the release profile obtained, the target release profile to be achieved was calculated to be NMT 30% after 2 hrs, 50-80% after 80 hrs, and NLT 80% after 16 hr. The initial batches F1 and F2 were formulated using varying concentration of hydrophobic polymer Ethylcellulose (Ethocelstd 10 premium EC) was used as a hydrophobic matrix agent which may be useful in controlled delivery of drugs. Formulation F1 released 70% of drug only within 24 hrs. In Formulation F2, a decrease in concentration of Ethocelstd 10 premium EC resulted in slight increase in cumulative release of 85% within 24 hrs. Formulations F3 to F5 were formulated using Ethylcellulose (Ethocelstd 45 premium EC) Formulation F3 released 35% of drug within 2 hours. In Formulation F4 and F5 a decrease in concentration Ethocelstd 45 premium EC was also not helpful in extending the release of drug. Formulations F6 to F9 were formulated using varying concentration of Eudragit RS 30D and Eudragit RSPO but cannot achieve extended release upto 24 hrs. So, further studies were carried out using Plasdone K 90 D as release retarding polymer.Formulations F10 to F13 were formulated using Plasdone K 90 D. Formulation F10 retarded the release and released only 32% within 24 hrs. Whereas in formulation F11 and F13 concentration of Plasdone K 90 D has been decreased and release was found to be 98% and 96% within 14 hrs. In formulation F12 concentration of Plasdone concentration was increased than F11 and attained a release of 98% within 24 hrs. The f2 value of formulation F12 was found to be 79%, the highest among all the batches prepared.

SUMMARY AND CONCLUSION

Nevirapine is a non-nucleoside reverse transcriptase inhibitor (NNRTI) drug which is used in thetreatment human immunodeficiency virus type 1 (HIV-1) infections. In this study Nevirapine Extended release tablets were prepared by using hydrophobic polymers. Thirteen formulations of extended release tablets of Nevirapine were developed by using Lactose Monohydrate and Micro crystalline cellulose as diluent and Magnesium stearate as lubricant in different proportions and varying grades of Eudragit, Ethyl Cellulose and povidone in different proportions. The formulation F12 was found to be best of all the formulations showing drug release matching the innovator product. The formulation F12 was evaluated for all the quality control tests. Stability study is carried out for 3 months at 25°C; 60% RH: and 40°C; 75%RH, according to ICH guidelines. The tablets were tested for drug release and percentage label claim during the stability period and confirmed that the results were found within the limits. The identified formula shall be utilized for the formulation development and other studies for successful launching of the product.

REFERENCES

1. Lee TWY, Robinson JR. Remington: the science and practice of pharmacy. 20th ed. Vols. 1069-70. MD: Lippincott Williams & Wilkins; 2000.
2. Loyd V, Allen J, Popovich NG, Ansel HC. Ansel: pharmaceutical dosage forms and drug delivery system. 8th ed. Philadelphia: Lippincott Williams & Wilkins; 2006. p. 260-75.
3. The theory and practice of industrial pharmacy. 3rd ed. 1986;171. Lea & Febiger, Philadelphia by Leon Lachman, Joseph L, Kanig.
4. Kiortsis S, Kachrimanis K, Broussali TH, Malamataris S. Drug release from tableted wet granulations comprising hydrophobic component. Eur J Pharm Biopharm. 2005;59(1):73-83. doi: 10.1016/j.ejpb.2004.05.004, PMID 15567304.
5. Korsmeyer RW, Lustig SR, Peppas NA. solute and penetrant diffusion in swellable polymers I. mathematical modeling. J Polym Sci B Polym Phys. 1986a;24(2):395-408. doi: 10.1002/polb.1986.090240214.
6. Bartoszynsti R, Powers Jd, Herderick EE. Pultz, T.a. statistical comparison of dissolution curves. Pharm Res. 2001;43(4):371-87.
7. Shah VP, Tsong Y, Sathe P, Liu Jp. In vitro Dissolution profile comparission. Statistics and analysis of the similarity factor f_2. Pharm Res. 1998;15(6):889-96. doi: 10.1023/A:1011976615750.
8. Stability testing of New Drug substances and Drug products (ICH-Q1A), September 1994. Stability testing of new dosage forms (ICH-Q1C), Sept 1994.
9. Guidelines for submitting documentation for the stability of human drugs and biologis (US FDA); February 1987.