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FORMULATION AND EVALUATION OF FAST DISSOLVING SUBLINGUAL LISINOPRIL TABLETS

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ABSTRACT:

The present study was carried out to develop the Lisinopril sublingual tablets Lisinopril were available in 5 & 10 mg. In the present study 10 mg strength were prepared and evaluated for all the physical parameters evaluation and in-vitro drug dissolution studies. In the innovator preparation, Sodium Bicarbonate and Sodium Carbonate were used and the restriction was laid to the use of both the buffers. So, the generic version was prepared by using single buffer sodium carbonate. Sublingual Tablets of this drug is very essential to overcome the lack of compliance associated with higher dose of conventional oral swallowing tablets and also to protect the drug degradation from hepatic metabolism which can result in undesired pharmacological action. In vitro dissolution was carried out by using USP Apparatus Type-II at 75 rpm, using 6.8 pH phosphate buffer as dissolution medium recommended by office of generic drugs (OGD). The effect of diluents and superdisintegrants on the disintegration time and content uniformity was clearly studied in this research. Special emphasis was laid on the pH of the tablet as restriction was laid in using both the buffer systems.

These sublingual tablets are used for treatment of insomnia. Sublingual tablets are developed because of their ease of administration and particularly insomniac patients will find great use of these sublingual tablets.

KEY WORDS: Lisinopril,Sublingual,Insomnia

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INTRODUCTION

Sublingual route (SR), faster than other routes except parenteral route, ensures that substance will degrade only by salivary enzymes before entering bloodstream, whereas orally administered drugs must survive through harsh environment of gastrointestinal tract (GIT). Lisinopril (1-[N2-{(S)-1-carboxy-3-phenylpropyl}-L-lysil]-L-proline dihydrate), an angiotensin-converting enzyme (ACE) inhibitor, is used in treatment of hypertension, which is caused by obesity, stress, decreased physical activity, increased salt intake and decreased calcium & potassium intake[1]. Lisinopril is very less bio available (25-30%) [2,3], due to incompletely absorption from GIT and first pass metabolism. SR offers fast disintegration of tablet, faster onset of action and rapid absorption by sublingual mucosa blood vessels [4,5]. Among different techniques (freeze drying technology[6,7], spray drying method, sublimation technology[8] and direct compression method [9] used for formulating sublingual tablets (STs), direct compression method does not require water or heat during formulation and is an ideal method. Excipients (super disintegrants) and spray dried form of excipients promote rapid disintegration and dissolution of tablet, giving faster onset of action. This study presents formulation and evaluation of STs of lisinopril for treatment of hypertension

EXPERIMENTAL SECTION

Materials

Lisinopril was obtained as a gift sample from Ranbaxy Pvt Ltd, Gurgaon, India. Pharmaburst®500, Ac-Di-Sol (Croscarmellose Sodium), Pearlitol (Mannitol) grades, Avicel pH101, L-HPC,DCP (Dicalcium phosphate) anhydrous, Na starch glycolate (SSG), Magnesium (Mg) stearate and talcum powder were obtained from Central drug house (CDH), New Delhi, India, and Aspartame was obtained from Himedia. All other chemicals used were of analytical grade, procured from standard sources.

Methods

Strategy I

The first strategy was to develop a formulation based on innovator composition. Pharmaburst is used as diluent in innovator composition. First a formulation was prepared without using buffer systems and then effect of buffer system on pH was studied.

Strategy II

The second strategy was developed by using mannitol and microcrystalline cellulose as diluents. In this strategy first buffer system is not used and then a single buffer system was incorporated and the difference of pH was observed.

Strategy III

The third strategy was developed by using F-Melt as diluent. In this strategy also first buffer system is not used and then a single buffer system was incorporated and the difference of pH

FORMULATION DESIGN AND DEVELOPMENT

Strategy I

Table No.1 Formulation Design of F1, F2

INGREDIENTS	F1(mg/tablet)	F2(mg/tablet)
Lisinopril	10	10
Pharmaburst®500	68.21	67.71
Crosscarmellose Sodium	4.50	3.50
PVP K30	-	1.50
Sodium Carbonate	8.00	8.00
Sodium Bicarbonate	11.00	11.00
Syloid 244 FP(Colloidal Silica)	1.50	1.50
Sucralose	0.25	0.25
Peppermint Flavour	0.25	0.25
Yellow Iron Oxide	0.25	0.25
Sodium Stearyl Fumarate	2.50	2.50

STRATEGY II

Table No.2 Formulation Design of F3, F4

INGREDIENTS	F3(mg/tablet)	F4(mg/tablet)
Lisinopril	10	10
Avicel PH 101	25.00	-
Avicel PH 102	-	30.96
Pearlitol SD 100 (Mannitol)	59.46	54.00
L-HPC	3.00	-
Crosscarmellose Sodium	3.00	4.00
PVP K30	-	1.50
Colloidal Silica	2.50	2.50
Sucralose	1.00	1.00
Peppermint Flavour	0.25	0.25
Yellow Iron Oxide	0.25	0.25
Sodium Stearyl Fumarate	2.00	2.00

Table No.3 Formulation Design of F5, F6,F7

INGREDIENTS	F5(mg/tablet)	F6(mg/tablet)	F7(mg/tablet)
Lisinopril	10	10	10
Prosolve SMCC90	25.00	25.00	20.00
Pearlitol SD200	61.96	29.00	24.75
Pearlitol 160C	-	31.46	30.46
Croscarmellose Sodium	3.50	3.50	4.50
PVP K30	-	1.50	1.50
Sodium Carbonate	-	-	10.00
Aerosil 200 (Colloidal Silica)	2.50	2.50	2.50
Sucralose	1.00	1.00	0.25
Peppermint Flavour	0.25	0.25	0.25
Yellow Iron Oxide	0.25	0.25	0.25
Sodium Stearyl Fumarate	2.00	2.00	2.0

STRATEGY III

Table No.4 Formulation Design of F8, F9,F10

INGREDIENTS	F8(mg/tablet)	F9(mg/tablet)	F10(mg/tablet)
Lisinopril	10	10	10
F-Melt	88.46	75.21	76.71
Crosscarmellose Sodium	-	4.00	4.50
PVP K30	-	1.50	1.50
Sodium Carbonate	-	10.00	8.00
Colloidal Silica	3.50	2.50	2.50
Sucralose	1.50	0.25	0.25
Yellow Iron Oxide	0.50	0.25	0.25
Peppermint Flavour	0.50	0.25	0.25
Sodium Stearyl Fumarate	2.00	2.50	2.50

Drug Excipient Compatibility Studies :-

Fourier transformed infrared (FTIR) spectra of lisinopril was taken by using the KBr disk method. The scanning range was 400 to 4000. The major peaks in recorded spectra were compared with standard spectra. These assignments are in full support of the given structures of drugs.

EVALUATION OF LISINOPRIL SUBLINGUAL TABLETS:-

Evaluation of Micromeritic Properties of Powder Blends

Angle of Repose:- The angle of repose has been used in several branches of science to characterize the flow of properties of solids. Angle of repose is a characteristic related to interparticulate friction or resistance to movement between particles. The angle of repose is calculated using the mentioned formula:-

$$\text{Angle of repose } (\alpha) = \tan^{-1} (h/r)$$

h = height of pile

r = radius of pile of powder

Bulk density :- It is the property of powders, granules and other "divided" solids, especially used in reference to mineral components (soil, gravel), chemical substances (pharmaceutical) ingredients, foodstuff or any other masses of corpuscular or particulate matter. It is defined as the mass of many particles of the material divided by the total volume they occupy. The total volume includes particle volume, inter-particle void volume and internal pore volume.

Tapped Density:- The tapped density is an increased bulk density attained after mechanically tapping a container containing the powder sample. Tapped density is obtained by mechanically tapping a graduated measuring cylinder or vessel containing a powder sample.

Measures of Powder Compressibility

Because the interparticulate interactions influencing the bulking properties of a powder are also the interactions that interfere with powder flow, a comparison of the bulk and tapped densities can give a measure of the relative importance of these interactions in a given powder.

Carr's index :- Carr's index was calculated using formula.

$$\text{Carr's Index} = 100*(TD-BD) / BD$$

A Carr index greater than 25 is considered to be an indication of poor flowability, and below 15, of good flowability.

Hausner's ratio:- It was also calculated from bulk density & tapped density & it indicates the flowability as well as compressibility of powder. The ratio was calculated using formula. The value below 1.25 indicates good flowability.

$$\text{Hausner's Ratio} = TD/ BD$$

PHYSICAL PARAMETERS EVALUATION OF TABLETS :-

Hardness Test:- This test is done to determine whether the tablets will be able to withstand the rigors of handling and transportation experienced in manufacturing plant, in the drug distribution systems and in the field at the hands of end users(patients/consumers)**.** Five tablets were randomly selected from each batch and hardness is determined by using digital ERWEKA hardness tester . The mean value of hardness was recorded.

Thickness:- Thickness was determined for five pre-weighed tablets of each batch using a Vernier, and the average thickness were reported.

Disintegration Time :- The disintegration test is performed to find out the time it takes for a solid oral dosage form like a tablet or capsule to completely disintegrate within the prescribed time when placed in a liquid medium. The time of disintegration is a measure of the quality. The disintegration time was determined by using electrolab disintegration time tester at 30 cycles/minute. 5 tablets were randomly selected and average was reported.

pH:- The pH of the tablet was measured by dissolving in 50 ml of water. Five tablets were randomly selected and average was reported.

Friability :- This test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap, or break. It determines the tablets ability to withstand mechanical stress, chipping, surface abrasion.

The friability was calculated using following formula.

$$\text{Friability} = 100*(W1 - W_2) / W_1$$

The friability test was conducted by using Roche friabilator, tablets equivalent to 6.5 grams were taken and drum was rotated for 100 times at 25rpm and the tablets were removed and dedusted and final weight was noted and friability was calculated by the mentioned formula. The friability limit is upto 1%.

Uniformity of Dosage Units

To ensure the consistency of dosage units, each unit in a batch should have a drug substance content within a narrow range around label claim.

Dosage units are defined as dosage forms containing a single dose or a part of a dose of drug substance in each unit. The uniformity of dosage units specification is not intended to apply to suspensions, emulsions, or gels in unit-dose containers intended for external, cutaneous administration.

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Weight Variation:- With a tablet designed to contain a specific amount of drug in a specific amount of tablet formula, the weight of tablet being made is routinely measured to ensure that a tablet contains the proper amount of drug.

As per USP the weight variation test is run by weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weights to the average. The tablets meet the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

Content Uniformity:- The CU test is used for tablets with less than 25mg of active ingredient and/or representing less than 25% total mass of tablet, 10 tablets were selected and assayed individually. The required specification for this test is that uniformity of dosage units should be within a range of 85-115% with Relative Standard Deviation of $\leq$ 6%

Wetting Time :- The wetting time of dosage form is related to contact angle. The wetting time of sublingual tablets is another parameter which needs to be assessed to give an insight into the disintegration properties of tablets. A lower wetting time implies quicker disintegration of tablet.

Water absorption ratio:- A piece of tissue paper folded twice is placed in a small petri-dish Containing 6 ml of water. A tablet was put on the tissue paper and Allowed to completely wet. The wetted tablet was then weighted. Water absorption ratio, R was
determined using following equation.

$$R = 100 \times \frac{Wa - Wb}{Wb}$$

Where, Wa = Weight of tablet after water absorption.
Wb = Weight of tablet before water absorption

Content Uniformity

Weigh 10 tablets and transfer individual tablets into 10 different 50 ml volumetric flasks and add 30 ml of diluent and sonicate for about 20 minutes and make upto the volume with diluents. Now filter it through 0.45µ PVDF filter and analyse for % drug content.

Assay

Determine average weight of 20 tablets. Weigh 10 tablets individually and transfer the tablets into 250 ml volumetric flask and add 150 ml of diluent and sonicate for about 20 minutes and make upto the volume with diluent. Centrifuge the solution at 6000 RPM for 5 minutes. Now filter the supernatant liquid through 0.45µ PVDF filter and analyse for % drug content.

In-Vitro dissolution Study:

Disolution Parameters

Volume	:	900 ml
RPM	:	75
Temperature	:	37$\pm$ 0.5°
USP Apparatus	:	Type II
Time points	:	1,3,5,7,10,13,15 minutes

Dissolution Test:-Perform the dissolution test for the sublingual tablets as per dissolution specifications. Withdraw 10 ml of aliquot sample by cannula fitted with 10µm prefilter and replace with fresh medium.

RESULTS AND DISCUSSIONS:

Drug Excipient Compatibility Studies :-

The possible chemical interaction of drug with polymer drug excipients compatibility was carried out for 3 weeks. At the end of three weeks pure drug, drug-excipients physical mixtures were analyzed by IR spectroscopy . The IR peaks in pure drug and drug excipients physical mixture are shown in figures 1 to 5. No changes in peaks this studies reveals the compatibility between drugs and excipients.

MICROMERITIC PROPERTIES OF POWDER BLEND

Pre compression parameters of granules were analysed, angle of repose values of all the formulations are in region of 27.6 ± 0.04 and 33.06 ± 0.04, bulk density was found to be in a range of 0.42 to 0.54 gm/cc, and tapped density was found to be in a range of 0.5 to 0.8 gm/cc, Cars index was found to be 10.86 to 50 , Hausner Ratio from1.1 to 1.5 % and Thus all the formulations were found to suitable for compression as tablets given in table 5 & 6 respectively.

PHYSICAL PARAMETERS

The lisinopril sublingual tablet formulations were subject to various post-compressive evaluation tests, such as hardness, thickness, disintegration time, friability, pH, wetting time water absorption ratio, weight variation,content uniformity, assay and Invitro drug dissolution release comparisons as followed for all the formulations were shown in Tables 7 to 15.

IN-VITRO DISSOLUTION STUDY:

Strategy I:-The first strategy was to develop a formulation based on innovator composition. The direct compression technique formulation (F2) resulted in segregation and finally led to poor content uniformity, assay on lower side, poor

flowability as carr's index was 36.36, so the wet granulation is preferred.

The wet granulation technique formulation (F2) ultimately led to formulation that has met all the requirements needed for a sublingual formulation. The Physical parameters were found to be within the limits and in-vitro drug release, assay values are also within the limits. Finally better content uniformity was achieved with the wet granulation technique. Now this formulation (F2) is taken as reference trial for developing the generic version avoiding all the patent issues.

The Dissolution Studies are also satisfactory for the innovator trials.

Strategy II:-The second strategy was developed by using the combination of Microcrystalline Cellulose & Mannitol. In this strategy, the formulation F3 was developed by direct compression by using Avicel pH 101 & Pearlitol SD100 along with superdisintegrants combination of croscarmellose sodium and low substituted hydroxypropyl cellulose. Even the formulation has content uniformity the assay was found on the lower side, poor flowability and higher disintegration time. So, the next plan was to shift for wet granulation formulation (F4).

The wet granulation formulation (F4) resulted in good content uniformity, assay values are in limits, but has poor flowability and also slightly higher disintegration time that is not a desired character for developing the generic version of innovator formulation as innovator formulation has disintegration time of less than 12 seconds.

The next formulation was developed by direct compression, this time by eliminating low substituted hydroxyl propyl cellulose and the diluents used are the combinations of Pearlitol SD200 and Prosolve SMCC 90 (Silcified MCC). This formulation (F5) resulted in poor flowability, assay was found to be on lower side and also poor content uniformity.

The above formulation design was changed to wet granulation and new formulation (F6) was developed. In this formulation, the diluents combinations are pearlitol 160C and pearlitol SD200 along with silicified MCC (Prosolve SMCC 90).This formulation although has good content uniformity and assay value within the limit, but has poor flowability and also slightly higher disintegration time.

A new formulation (F7) was designed by incorporating Sodium bicarbonate (as single buffer system) to the above formulation and evaluated for all the parameters. The flowability was improved but the disintegration time was increased which is not a desired character for developing the generic version for the innovator drug. All the formulations have satisfactory drug release within 30 minutes of dissolution studies.

Strategy III :-The next strategy was developed by using F-melt as diluent to improve the flowability and maintaining the content uniformity.

The F8 formulation was developed by direct compression and evaluated for the physical parameters and it was found that the flow property was improved but the content uniformity was not good, so wet granulation was preferred and new formulation was designed.

The F9 formulation was made by wet granulation technique and evaluated for physical parameters and the flow property was improved along with content uniformity, but has slightly higher disintegration time, so the next formulation was designed in such a way that disintegration time has to be improved by increasing the superdisintegrtant concentration and final reproducible batch was taken and evaluated for all the physical parameters, assay and content uniformity.

The final reproducible batch (F10) was found to have good flow properties, content uniformity and assay was found to be within limits. The dissolution studies also correlated with that of the innovator drug shown in table 16 and figures 6-16.

CONCLUSION:

The innovator sublingual tablets of 10mg strength was successfully prepared by using single buffer system containing Sodium Carbonate. The final optimized formulation F10 was evaluated for all physical parameters and in-vitro drug release. The optimized formula F10 is the best competitive generic version for the Innovator formulation. All the physical evaluation parameters and in-vitro drug release patterns are found to compete with that of the innovator preparation and also faster disintegration time was achieved with the optimized formula that competes with the innovator formulation.

Table 5 Micromeritic Properties of powder blend

Strategy	Formulation code	Parameters	
		Angle of repose	Flow Property
Strategy I	F1	33.06	Good
	F2	28.8	Excellent
Strategy II	F3	32.2	Good
	F4	30.96	Good
	F5	30.96	Good
	F6	29.2	Excellent
	F7	27.6	Excellent
Strategy III	F9	32.6	Good
	F9	30.5	Good
	F10	29.6	Excellent

Table 6 Micromeritic Properties of powder blend

Strategy	Formulation code	Parameters				
		Bulk Density	Tapped Density	Carr's Index	Hausner's Ratio	Flow Property
Strategy I	F1	0.44	0.6	36.36	1.36	Very Poor
	F2	0.46	0.51	10.86	1.1	Good
Strategy II	F3	0.49	0.66	34.69	1.34	Very Poor
	F4	0.44	0.59	34.09	1.34	Very Poor
	F5	0.54	0.8	48.14	1.48	Very Poor
	F6	0.42	0.63	50	1.5	Very Poor
	F7	0.43	0.5	16.27	1.16	Fair
Strategy III	F8	0.43	0.52	20.93	1.2	Passable
	F9	0.45	0.51	13.33	1.13	Good
	F10	0.44	0.51	15.9	1.15	Good

Table 7 Physical parameters evaluation Observations

Strategy	Formulation code	Parameters		
		Hardness (Newtons)	Thickness(mm)	Disintegration Time(Seconds)
Strategy I	F1	34	2.41	10.8
	F2	29	2.33	11.4
Strategy II	F3	29.8	2.53	14.8
	F4	25	2.48	15.2
	F5	31	2.46	11.4
	F6	31.2	2.36	16.2
	F7	24.2	2.36	21.2
Strategy III	F8	32.8	3.43	17.6
	F9	29	3.53	13.8
	F10	24.6	2.42	12.3

Table 8 Physical parameters evaluation Observations

Strategy	Formulation code	Parameters		
		Friability(%)	pH	Wetting Time (seconds)
Strategy I	F1	0.11	6.70	11.6
	F2	0.09	10.38	50.8
Strategy II	F3	0.21	6.77	35.8
	F4	0.13	6.63	46
	F5	0.25	6.58	20.2
	F6	0.19	6.78	37.4
	F7	0.29	10.68	35.4
Strategy III	F8	0.1	6.02	34.2
	F9	0.17	10.34	54.2
	F10	0.1	10.31	51.6

Table 9 Water Absorption Ratio Observations

Strategy	Formulation code	Parameters		
		Initial weight(mg)	Final weight(mg)	Water absorption ratio
Strategy I	F1	101.91	178.28	74.93
	F2	102.74	162.06	57.7
Strategy II	F3	101.50	181.23	78.55
	F4	101.65	175.45	72.60
	F5	102.50	167.34	82.77
	F6	101.81	199.96	96.40
	F7	101.34	189.34	86.83
Strategy III	F9	101.56	182.06	79.26
	F9	102.80	137.34	33.59
	F10	102.13	165.83	62.37

Table 10 Weight variation Observations

Strategy	Formulation code	Average Weight of 20 Tablets	Minimum Weight(mg)	% Difference to the average	Maximum Weight(mg)	% Difference to the average
Strategy I	F1	100.73	98.89	-1.82	102.12	+1.37
	F2	100.76	98.37	-2.37	102.56	+1.78
Strategy II	F3	100.75	98.27	-2.46	102.76	+2.76
	F4	100.80	98.23	-2.54	102.66	+1.84
	F5	100.99	98.21	-2.75	102.86	+1.85
	F6	100.94	98.31	-2.6	102.96	+2.0
	F7	101.03	98.29	-2.71	102.89	+1.84
Strategy III	F8	100.97	98.19	-2.7	102.99	+2.00
	F9	100.97	98.59	-2.35	102.96	+2.96
	F10	101.09	98.22	-2.83	102.93	+1.82

Strategy I

Table 11 Content Uniformity of Formulation Trials F1 & F2

Sr.No.	F1		F2	
	mg/tablet	% drug content	mg/tablet	% drug content
1	9.60	87.4	9.55	101.4
2	9.7	87.7	9.23	92.3
3	8.98	85.1	9.57	102.0
4	9.08	88.0	9.64	104.0
5	8.88	82.3	9.19	91.1
6	9.06	87.4	9.40	97.1
7	8.94	84.0	9.24	92.6
8	9.96	84.6	9.36	96.0
9	9.07	87.7	9.58	102.3
10	8.99	85.4	9.23	92.3
Minimum	8.88	82.3	9.19	91.1
Maximum	9.08	88.0	9.64	104.0
AVERAGE	9.00	86.0	9.39	98.5
%RSD	-	2.27	-	5.09

Strategy II :-

Table 12 Content Uniformity of Formulation Trials F3 & F4

Sr. No.	F3		F4	
	mg/tablet	% drug content	mg/tablet	% drug content
1	9.06	87.4	9.64	104.0
2	9.47	99.1	9.47	99.1
3	8.98	85.1	9.63	103.7
4	9.58	102.2	9.47	99.1
5	9.28	93.7	9.42	97.7
6	9.36	96.0	9.57	102.0
7	8.94	84.0	9.62	103.4
8	8.96	84.6	9.55	101.4
9	9.37	96.2	9.57	102.0
10	8.99	85.4	9.62	103.4
Minimum	8.94	84.0	9.42	97.7
Maximum	9.58	102.2	9.64	104.0
AVERAGE	9.19	91.3	9.55	101.58
%RSD	-	7.07	-	2.19

Table 13 Content Uniformity of Formulation Trials F5 to F7

Sr.No.	F5		F6		F7	
	mg/tablet	% drug content	mg/tablet	% drug content	mg/tablet	% drug content
1	8.62	74.9	9.66	104.6	9.70	105.7
2	8.94	84	9.66	104.6	9.55	101.4
3	9.17	90.6	9.51	100.3	9.64	104.0
4	9.01	86	9.47	99.1	9.57	102.0
5	8.80	80	9.53	100.9	9.61	103.1
6	8.46	70.3	9.50	100	9.75	107.1
7	9.03	86.6	9.34	95.4	9.61	103.1
8	8.62	74.9	9.39	96.9	9.56	101.7
9	8.54	72.6	9.53	100.9	9.55	101.4
10	8.64	75.4	9.47	99.1	9.56	101.7
Minimum	8.46	70.3	9.34	95.4	9.55	101.4
Maximum	9.17	90.6	9.66	104.6	9.75	107.1
AVERAGE	8.78	79.5	9.506	100.18	9.61	103.1
%RSD	-	8.66	-	2.90	-	1.89

Strategy III :-

Table 14 Content Uniformity of Formulation Trials F8 to F10

Sr.No.	F8		F9		F10	
	mg/tablet	% drug content	mg/tablet	% drug content	mg/tablet	% drug content
1	9.34	95.4	9.43	98.0	9.33	95.1
2	9.45	98.6	9.25	92.9	9.39	96.9
3	9.31	94.6	9.34	95.4	9.31	94.6
4	9.30	94.3	9.48	99.4	9.34	95.4
5	9.25	92.9	8.76	78.9	9.33	95.1
6	9.29	94.0	9.45	98.6	9.37	96.3
7	9.35	95.7	9.49	99.7	9.38	96.6
8	9.24	92.6	9.47	99.1	9.35	95.7
9	9.27	93.4	9.40	97.1	9.35	95.7
10	9.30	94.3	9.35	95.7	9.24	92.6
Minimum	9.24	92.6	8.76	78.9	9.24	92.6
Maximum	9.45	98.6	9.49	99.7	9.39	96.9
AVERAGE	9.31	94.58	9.34	98.5	9.33	95.4
%RSD	-	1.82	-	6.49	-	1.27

Table 15 Assay Results

STRATEGY	FORMULATION CODE	ASSAY (%)
Strategy I	F1	86.3
StrategyII	F2	98.6
	F3	94.3
	F4	90.9
	F5	76.6
	F6	98.3
	F7	103
Strategy III	F8	86.9
	F9	97.7
	F10	100.1

Table 16 Dissolution Results

Strategy	Formulation code	% Drug Release With Time(Minutes)						
		1	3	5	7	10	15	30
Strategy I	F1	57.4	66.8	71.7	74.2	77.5	80	82.9
	F2	45.7	71.6	78.8	81.9	84.5	87	95.4
Strategy II	F3	51.1	66.3	81.1	85.2	88.7	90.4	94.3
	F4	26.7	51.6	67.5	74.3	81.9	86.7	92.3
	F5	59.9	69.4	73.6	75.1	77.3	79.4	81.9
	F6	64.7	87.8	91.4	92.8	94	95.3	96.9
	F7	51.6	60.4	70.3	77.6	84.2	89.8	93.1
Strategy III	F8	81.2	86	86.6	89.6	91.3	92.7	95.3
	F9	49.2	73.6	81.4	85.4	88.8	91.8	95.6
	F10	49.3	77.7	84.1	86.8	89.4	92.5	94.9

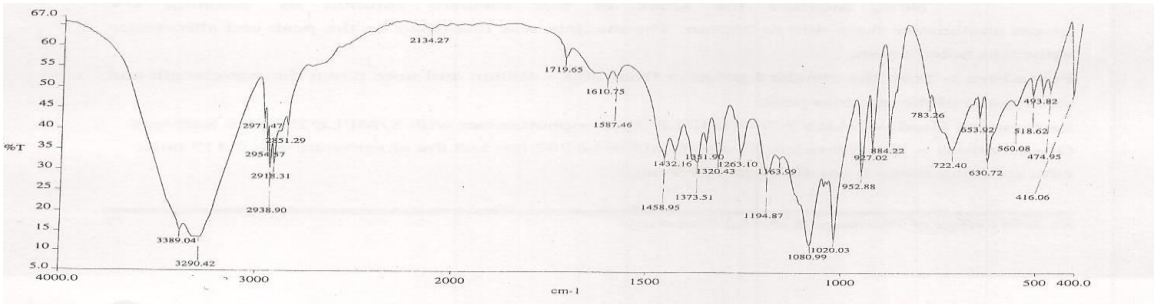

Figure 1 FT-IR Graph of API

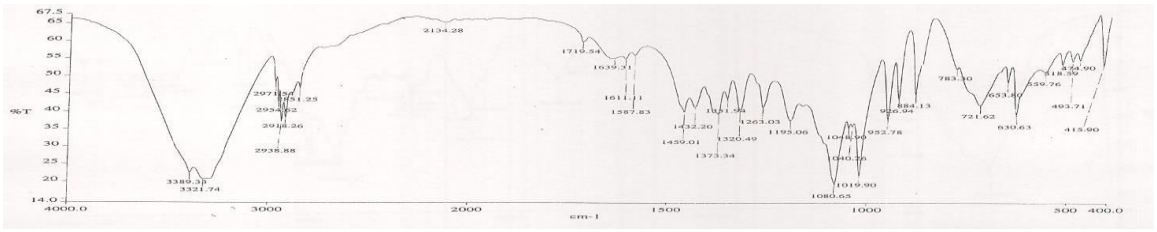

Figure 2 FT-IR Graph of L-HPC+Croscarmellos Sodium+MCC+Mannitol

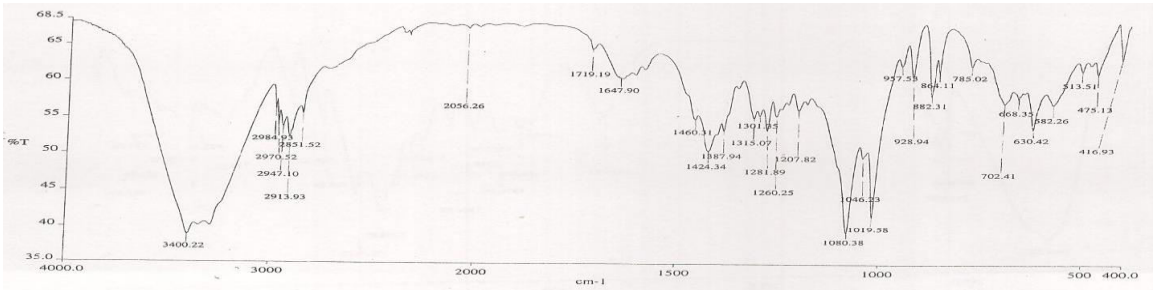

Figure 3 FT-IR Graph of Croscarmellose Sodium+MCC+Mannitol+PVP K30

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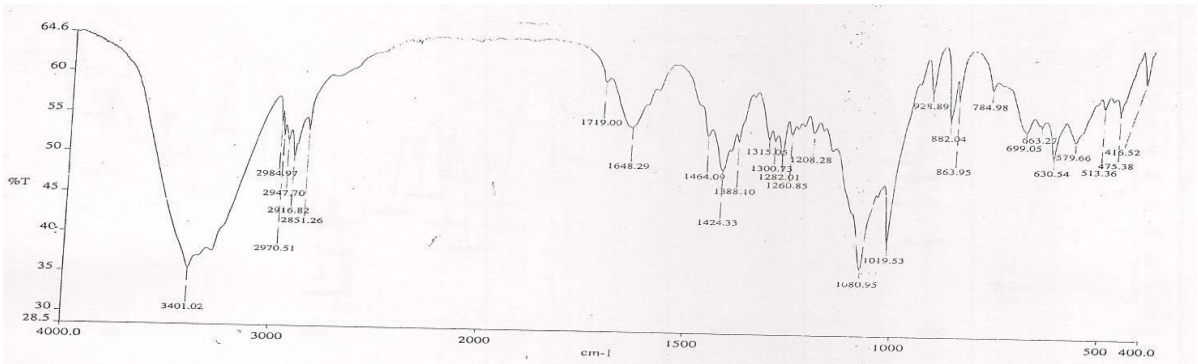

Figure 4 FT-IR Graph of F-Melt+Croscarmellose Sodium+Buffering agent+ PVP K30

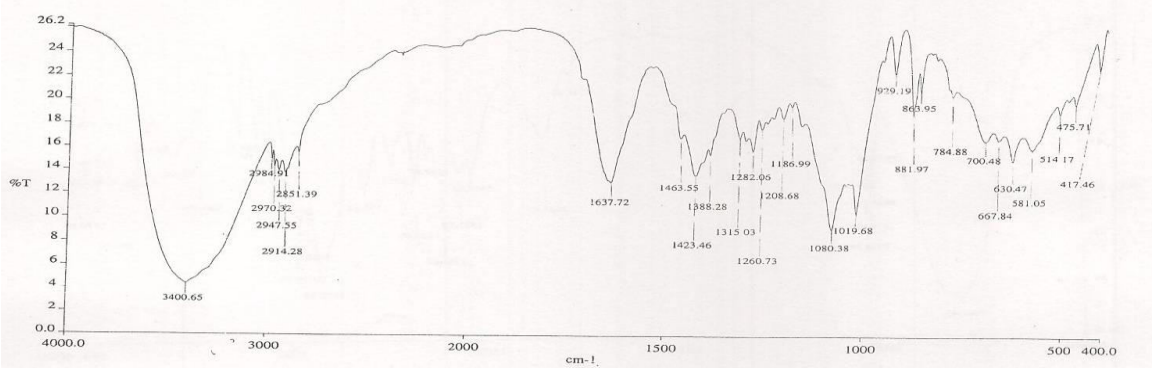

Figure 5 FT-IR Graph of API+ F-Melt+Croscarmellose Sodium+Buffering agent +PVP K30

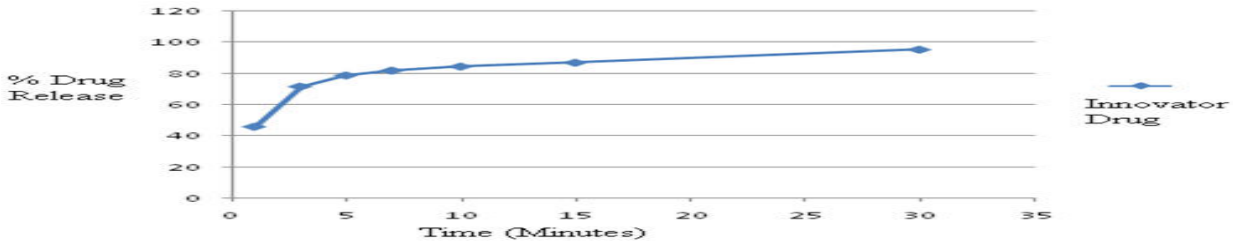

Figure 6 Disolution Profile of Innovator Drug

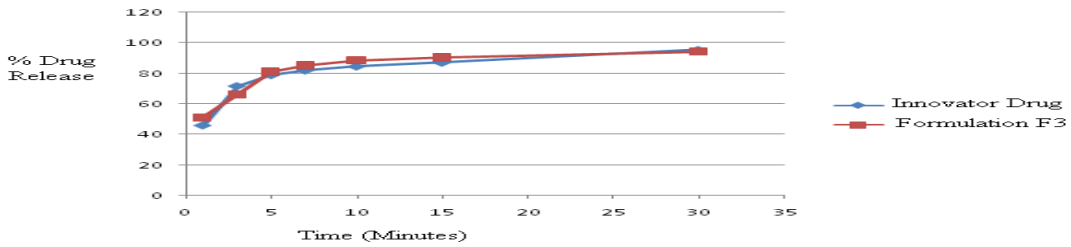

Figure 7 Comparion of Dissolution Profile of Formulation F3 with Innovator

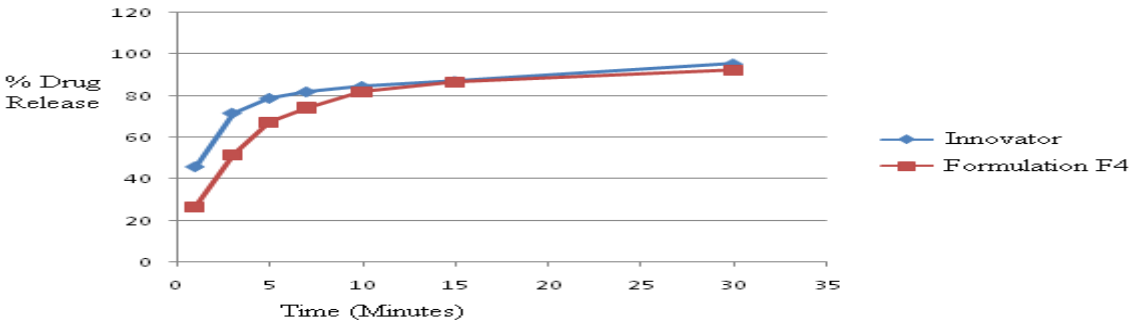

Figure 8 Comparion of Dissolution Profile of Formulation F4 with Innovator

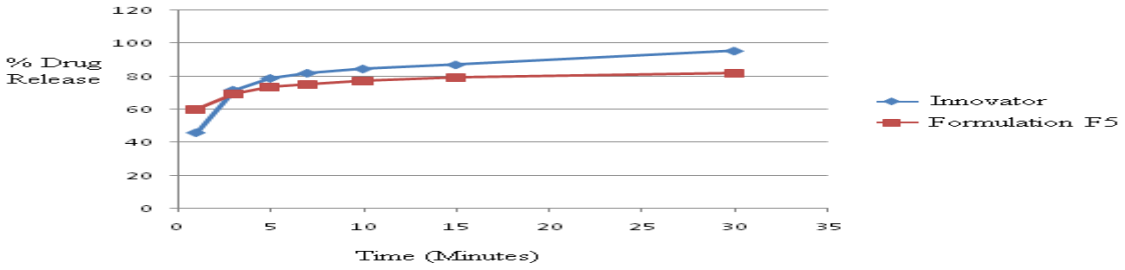

Figure 9 Comparion of Dissolution Profile of Formulation F5 with Innovator

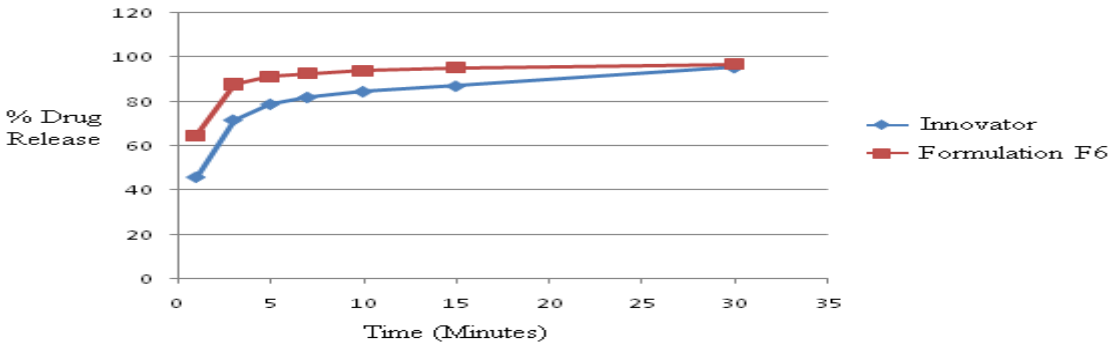

Figure 10 Comparion of Dissolution Profile of Formulation F6 with Innovator

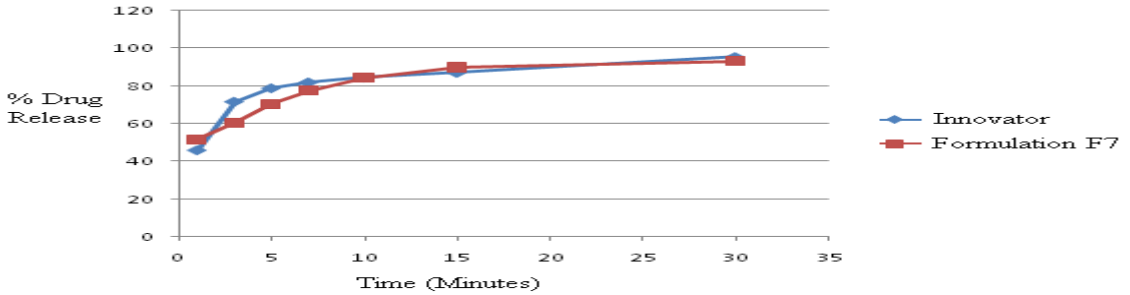

Figure 11 Comparison of Dissolution profile of Innovator Drug & Formulation F7

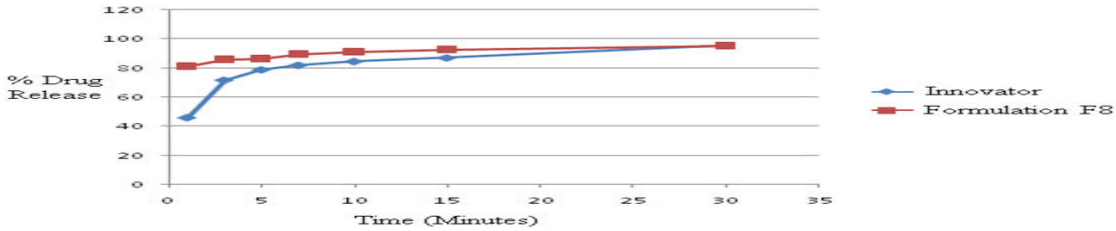

Figure 12 Comparison of Dissolution profile of Innovator Drug & Formulation F8

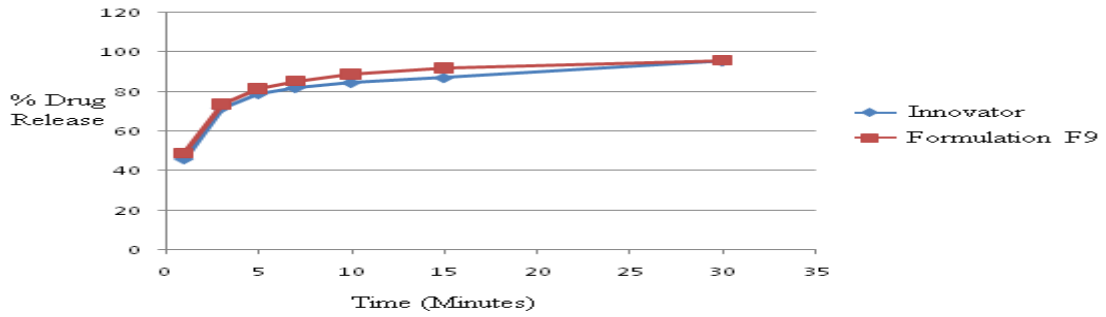

Figure 13 Comparison of Dissolution profile of Innovator Drug & Formulation F9

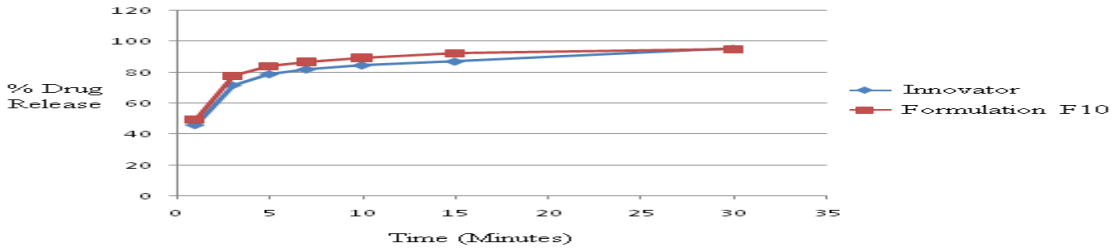

Figure 14 Comparison of Dissolution profile of Innovator Drug & Formulation F10

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