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Formulation and Analysis of Anti-Hypertensive Immediate-Release Tablets

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Keywords

Nebivolol hydrochloride, Hypertension, Direct compression, Immediate release tablets

Abstract

Nebivolol hydrochloride is a highly selective beta-blocker that causes vasodilation. This study addresses the use of various superdisintegrants such as Crosspovidone and croscarmellose sodium. Compounding was done using the direct compression method. Superdisintegrants are used in immediate release tablet formulations to improve disintegration and dissolution and provide a more rapid onset of action. Drug-excipient interactions were studied by FT-IR. Manufactured tablets were tested for various parameters before and after compression. Bulk density, tamped density, weight change, thickness, brittleness, disintegration time, dissolution studies, etc. Finally, it was concluded that the F-2 formulation had the highest release potential.

Introduction

The most common forms of oral medications are tablets or capsules. Tablets are solid dosage forms it contains single or multiple active components in a unit dose. The tablets are meant to be consumed orally. Many patients have required a rapid commencement of action in a variety of therapy circumstances, necessitating immediate release. [1].

Excipients may include binders, slides and lubricants to provide effective compression and disintegrating agents to promote tablet breakdown in the gastrointestinal tract. Instant release tablets. Instant release tablets were invented to disintegrate and release their dosage type without any special rate control options like special coatings and different techniques. Recently, immediate release drugs have begun to gain popularity because of their ease of use and better patient adherence [2].

The oral route is one of the most sought after routes because of its systemic effectiveness, ease of administration, simplicity, safety, convenience, non-invasiveness, flexibility and most importantly patient satisfaction. Oral solid delivery systems are manufactured at a lower cost because aseptic conditions are not required [3].

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The intended dosage form of the tablet is to swallow the tablets whole, break them up, and release them rapidly and forcefully in the gastrointestinal tract. During the entire course of treatment, scientists have recently focused their attention on the words where the pill is immediately released. Attempts to develop rapidly disintegrating tablets have been completed using appropriate diluents and super dissolves [4,5]

Materials And Methods [6-8]

Nebivolol hydrochloride, sodium carmellose cross, povidone cross, lactose, and nebivolol hydrochloride instant tablets are prepared by direct compression. Accurately weigh 20 mg of nebivolol mixed with super solutes and with properly weighed diluents and slips. In this method, the tablets are punched directly in the tablet press.

Table 01: Formulation of Nebivolol Hydrochloride Immediate release Tablet

Ingredients	Ingredient					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
Nebivolol Hcl(mg)	20	20	20	20	20	20
Cross carmellose (mg)	10	15	10	-	-	-
Cross povidone(mg)	-	-	-	10	15	20
Sodium starch glycolate (mg)	30	30	30	30	30	30
Sodium lauryl sulphate (mg)	6	6	6	6	6	6
Talc (mg)	2	2	2	2	2	2
Lactose (mg)	132	127	132	132	127	122
Total weight(mg)	200	200	200	200	200	200

Preformulation

Determination of Maximum wavelength (Max) [9, 10]-

To make a 10 g/ml Nebivolol HCL standard stock solution, dissolve 10 mg of Nebivolol HCL in 5 ml of methanol and dilute with pH 6.8 phosphate buffer to 10 ml. The stock solution was then diluted further with buffer solution with concentration of 10 g/ml. A UV spectrophotometer was used to measure the maximum wavelength of the produced solution in the range of 200 to 400 nm.

Preparation of UV Calibration curve [11, 12]-

By using a UV spectrophotometer, the absorbance of this solution is determined at a certain wavelength. To obtain the standard curve, a calibration curve is plotted on the graph.

Drug- excipients compatibility studies [13, 14]-

Studies using Fourier Transform Infrared (FTIR) spectroscopy Using an IR spectrophotometer, FT-IR spectra of the pure drug and physical combination of ticagrelor were captured. In KBr dishes, the samples were prepared, and they were scanned at 400 to 4000 cm-1.

Pre Compression parameters for immediate release [15-20]

Angle of repose

The evaluation criterion that depends on inter-particle cohesiveness is the angle of repose. Less cohesion between the particles gives the powder better flow characteristics. Surface tension, electrostatic forces, and non-specific van der Waals forces that result from contact or friction with the equipment's wall are the causes of inter particle cohesive forces.

Angle of repose can be determined by using the formula

$\tan \theta = h / r$

Where,

h= height of cone,

r= radius of cone,

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Bulk Density

The following equation was used to calculate the bulk density:

Bulk density = INITIAL WEIGHT BULK VOLUME

Tapped Density

Using the tapping method and a measuring cylinder filled with a measured amount of powder, the tapped density was calculated. The following calculation was used to compute the tapped density.

Tapped density = MASS OF POWDER TAPPED VOLUME OF POWDER

Carr's Compressibility Index

It is calculated by using following equation.

% COMPRESABILITY INDEX= TD-BDTDX 100

Where,

TD- Tap Density,

BD- Bulk Density

Hausner's Ratio

The hausner's ratio can be used to define a comparable index to represent the flow characteristics. The following formula can be used to compute the Hausner's ratio:

Hausner's ratio = TAPPED DENSITYBULK DENSITY

POST COMPRESSIONAL EVALUATION PARAMETERS OF IMMEDIATE RELEASE TABLETS [21- 30]

General appearance

The basic aesthetics of a tablet, its visual identity, and its overall "elegance" are crucial for consumer adoption.

Tablet Thickness and Diameter analysis-

In recreating appearance, tablet thickness is a crucial factor. A straightforward approach can be used to measure tablet thickness and diameter. Using a computerised Vernier calliper, the diameter and thickness of 5 tablets were measured.

Hardness analysis -

Tablet hardness was measured by Monsanto Hardness tester.

Drug Content

Ten tablets are chosen at random from the formulation, ground into a fine powder, and the mg of medicine in the powder is precisely measured before being transferred to 100 ml volumetric flasks with the appropriate pH solution. The volume is raised to the required level using filtration and a solution. After the filtrate has been properly diluted, the concentration of pharmaceuticals in one ml of the filtrate is assessed using a single beam UV spectrophotometer.

Weight variation-

To check for consistency in weight, the weights of the twenty tablets were computed both individually and collectively using a computerized weighing scale.

Table 02: The Weight variation Parameter

Average weight of tablet	% deviation allowed
80mg or less	±10
60mg-250mg	±7.5
250mg - more	±5

Friability study

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Tablet friability is evaluated using the Roche Friabilator. A random selection of 20 tablets are made from each formulation. The 20 pills are first placed in the Friabilator at their calculated starting weight. The Friabilator rotates 100 times at a speed of 25 rpm in 4 minutes. The% friability is calculated using the formula below:

F= Initial weight-Final weight Final weightX100

Disintegration time

There is developed a comparatively straightforward method with strict requirements. This tablet evaluated by Disintegration apparatus. The time it takes for the tablet to completely dissolve is then visually seen and timed using a stopwatch.

In-vitro study-

A dissolution research using 500 mL of phosphate buffer (pH 6.8) as the dissolution media was carried out at 50 rpm in a USP II paddle-type apparatus. Utilizing a UV-Visible Spectrophotometer, the materials were properly diluted before being measured spectrophotometric at 272.2 nm. The dissolving tests were performed three times. To establish an adequate time limit for tablet disintegration, the dissolving parameters and isolation rates of all candidate formulations were calculated.

Table 03: The *In-vitro* study Parameter

Parameter	Specification
Apparatus	USP II
Dissolution medium	Phosphate buffer pH 6.8
Rotational Speed	50 rpm
Temperature	37 °c
Sample Withdrawn	5.0ml
Sampling interval	5.00min
Absorbance measured	291 nm

Result & Discussion

Table 04: Calibration curve data for nebivolol hydrochloride immediate release tablet

Concentration	Absorbance
2	0.125
4	0.290
6	0.498
8	0.682
10	0.862

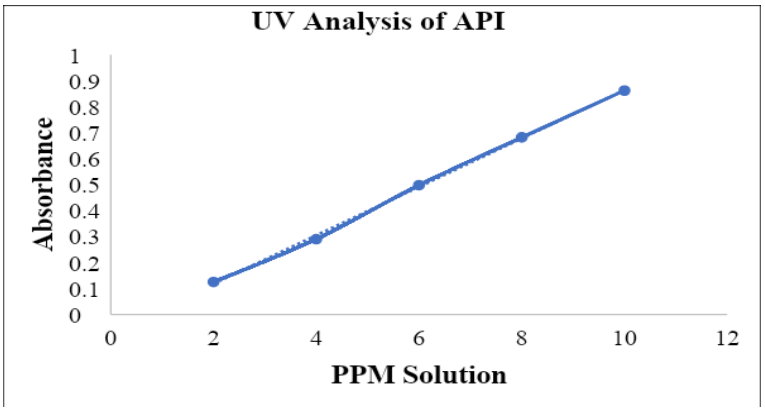

Figure 1: Calibration Curve of API

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FTIR Study-

Drug compatibility study was done with the help of FTIR. The IR spectrum of pure Nebivolol hydrochloride compared with as Nebivolol Hcl + croscarmellose, Nebivolol Hcl + cross povidone. This shows that there is no any significant interaction between drug and polymers.

1. FTIR study of pure drug (Nebivolol Hcl)

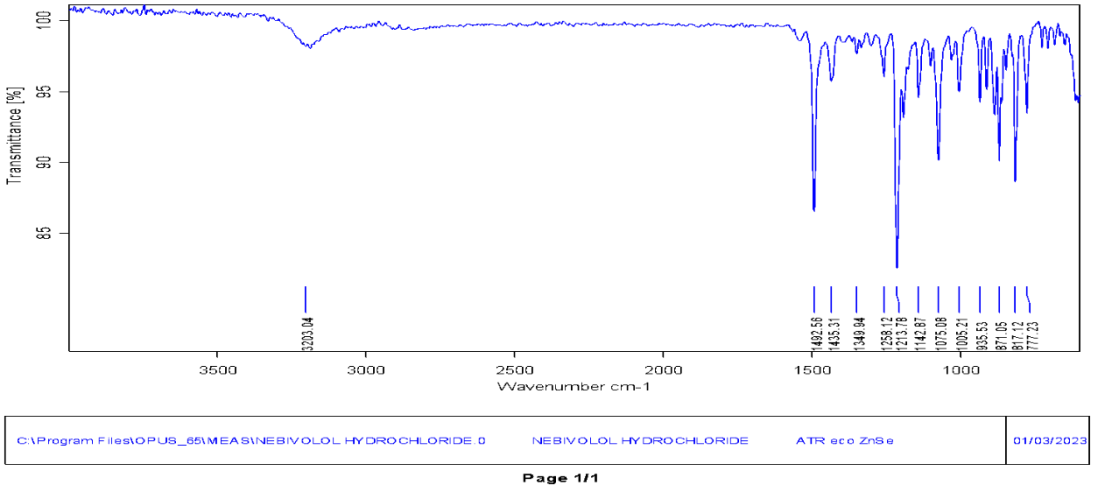

Figure 2: Spectrum of Nebivolol Hcl

2. Nebivolol Hcl + Croscarmellose

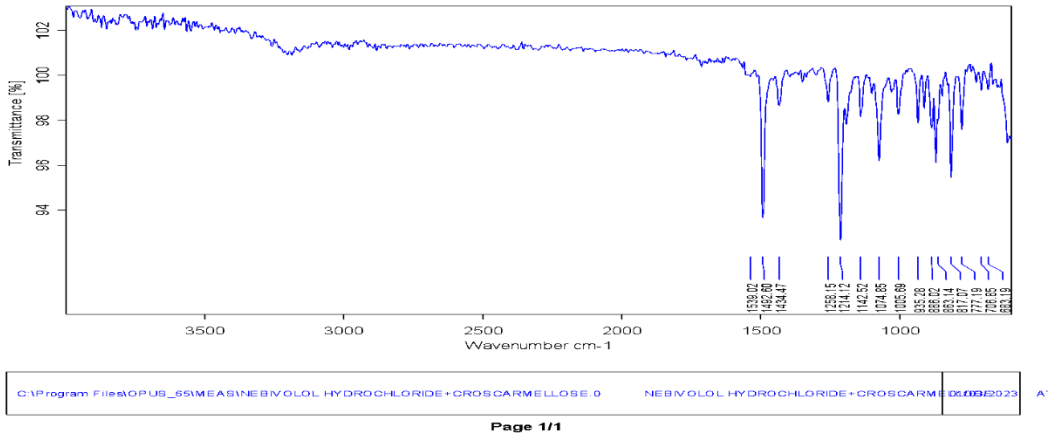

Figure 3: FTIR spectrum of Nebivolol+ Croscarmellose

3) Nebivolol Hcl + Crospovidone

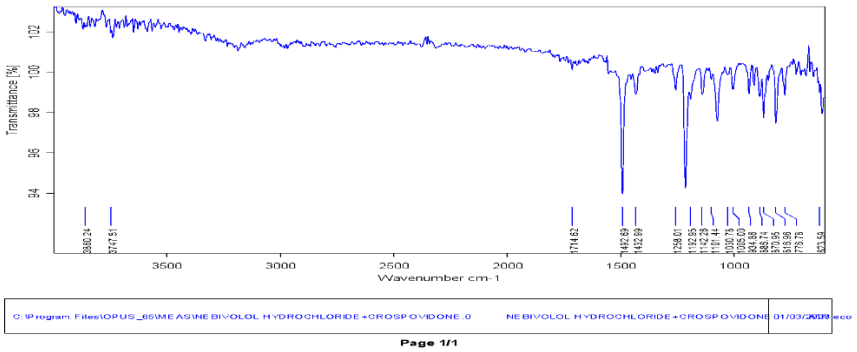

Figure 04 FTIR Spectrum of Nebivolol+ Crosspovidone

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Pre compression Parameter-

Table 5: Pre Compression parameter for immediate release table

Formulation	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Hausner ratio	Compressibility index	Angle of repose
F1	0.460	0.540	1.97	16.24	20.9
F2	0.462	0.450	1.29	16.19	20.07
F3	0.410	0.516	1.46	20.17	20.23
F4	0.416	0.540	1.32	21.87	21.47
F5	0.420	0.510	1.30	21.01	24.40
F6	0.421	0.520	1.30	21.24	20.14

The Pre-compression parameters have been performed as per Indian pharmacopeia & its specifications, so all the observation of the parameter has complied with the standard. So consider that all formulations of mixture powder has good follow ability & packing capacity as per the given table.

Evaluation of post-compression parameters-
Weight Variation-

Table 06- Weight variation record of different formulation

Sr. No	**Tablet**	**Weight of Tablet (mg)**					
		F1	**F2**	**F3**	**F4**	**F5**	**F6**
1	T1	200	200	200	200	200	200
2	T2	200	200	200	200	200	200
3	T3	201	201	198	202	202	201
4	T4	200	200	200	200	200	200
5	T5	200	200	200	200	200	200
6	T6	200	201	198	202	201	200
7	T7	200	200	200	200	200	200
8	T8	200	200	200	200	200	200
9	T9	200	198	202	200	200	200
10	T10	198	202	201	200	200	200
11	T11	201	200	199	200	200	201
12	T12	202	200	200	200	200	201
13	T13	198	201	198	200	200	200
14	T14	200	200	200	200	200	200
15	T15	200	200	200	200	200	200
16	T16	200	200	200	200	200	200
17	T17	200	200	200	200	200	200
18	T18	200	200	200	200	200	200
19	T19	201	201	201	200	200	200

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20	T20	200	199	200	200	200	200
Total weight		4001	4003	3997	4004	4003	4003
Averages weight		200.05	200.15	199.85	200.2	200.15	200.15
Upper limit		202	202	202	202	202	201
Lower Limit		198	198	198	200	200	200
% Variation		**1.9995**	**1.9985**	**2.0015**	**0.999**	**0.99925**	**0.49963**

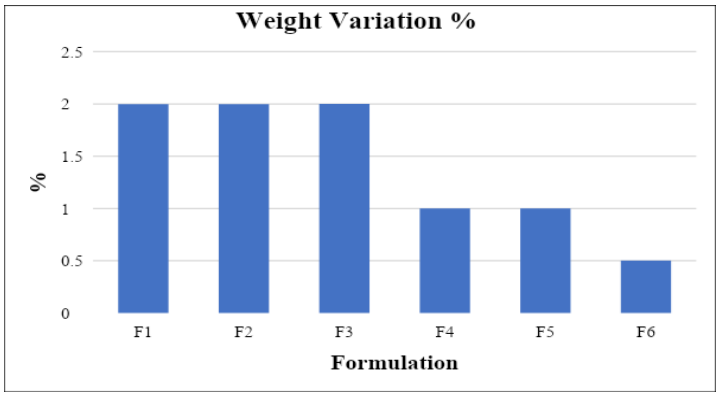

Figure 5: Weight variation graphical presentation

Hardness-

Table 7: Hardness of the different formulation

Formulation	Hardness (kg/cm2)
F1	3.5
F2	2.5
F3	2.8
F4	2.9
F5	3.1
F6	3.3

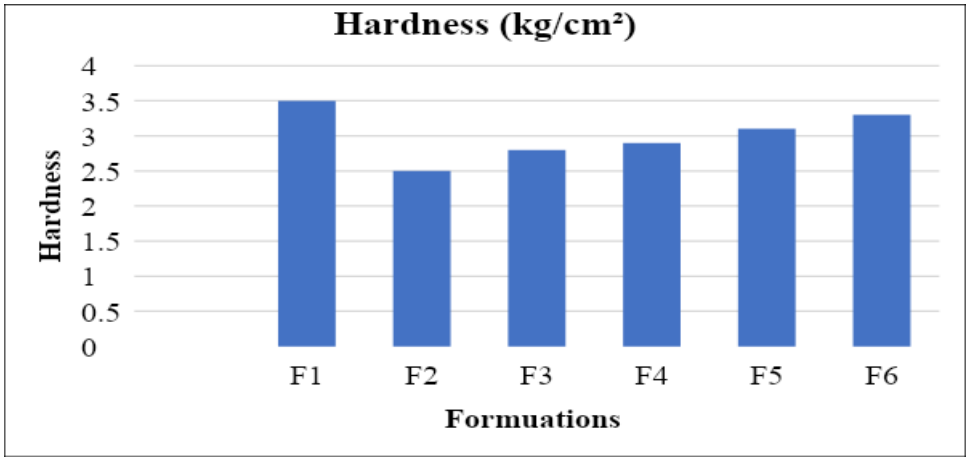

Figure 6: Hardness of different formulation.

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Friability-

Table 08 : The Friability of the different formulation

Formulation	Friability (%)
F1	0.36
F2	0.32
F3	0.28
F4	0.4
F5	0.38
F6	0.3

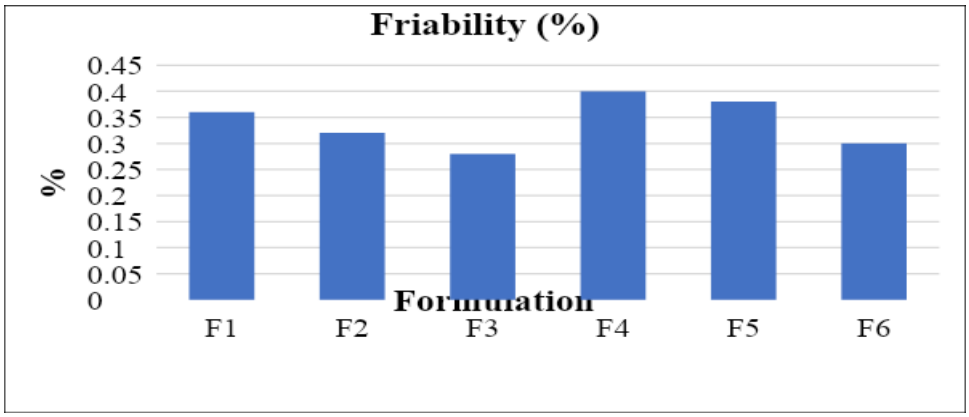

Figure 7: Graphical Presentation of Friability

Thickness

Table 09: The table contain the observations of thickness

Formulation	Thickness (mm)
F1	2.8
F2	2.72
F3	2.69
F4	2.81
F5	2.71
F6	2.72

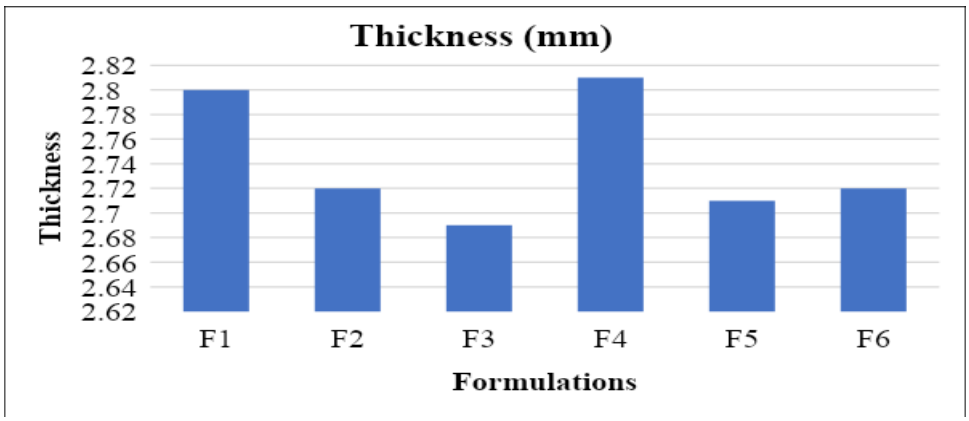

Figure 08 - The Graphical Presentation of Thickness

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Disintegration time-

Table 10: Disintegration study of all formulation

Formulation	Disintegration time (sec)
F1	30
F2	12
F3	15
F4	21
F5	24
F6	25

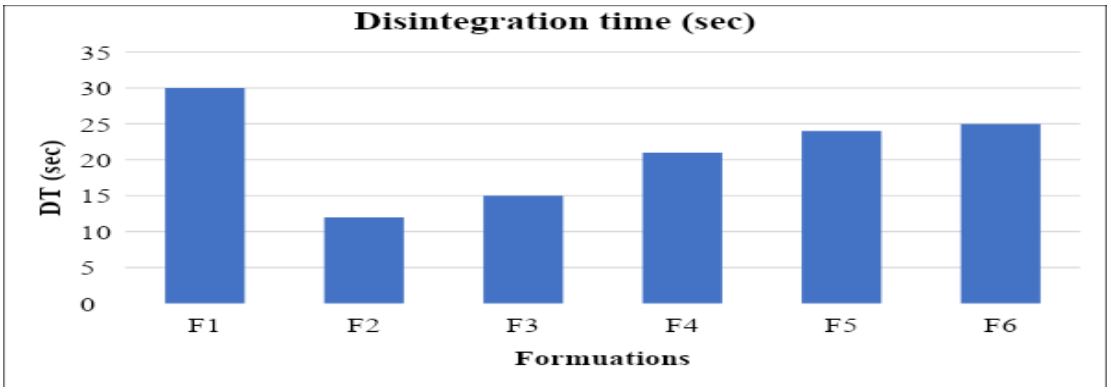

Figure 9: The disintegration time of different formulation

Drug Content:

Table 11- The drug content in the formulations

Formulations	Drug Content (%)
F1	**94.83**
F2	98.68
F3	95.45
F4	93.56
F5	95.12
F6	88.6

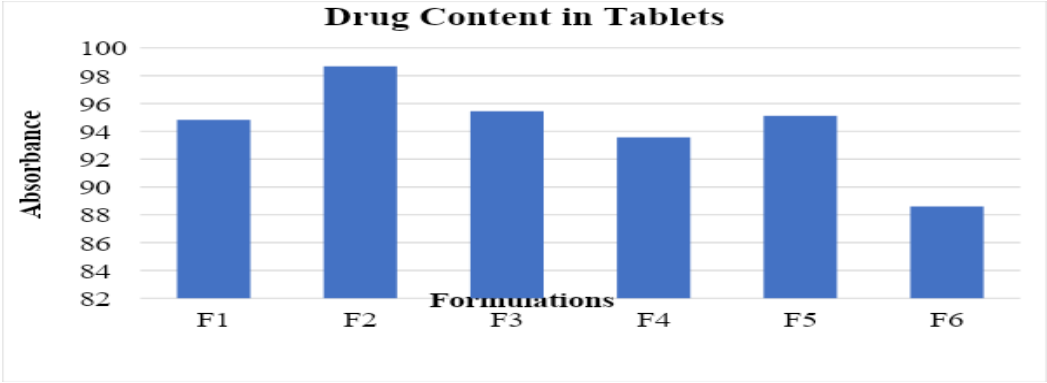

Figure 10 - The graphical presentation of drug content of different formulation

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***In vitro* study-**

Table 12- The *In vitro* study record

Time (min)	F1	F2	F3	F4	F5	F6
5	28.978	35.341	22.456	34.609	45.341	28.764
10	43.438	43.315	27.498	37.628	53.315	32.342
15	64.593	58.897	33.568	41.893	78.897	45.872
20	83.764	74.612	81.367	83.623	84.612	57.562
25	86.38	94.554	84.735	86.478	94.554	69.376
30	90.42	96.62	89.82	87.56	92.62	75.599

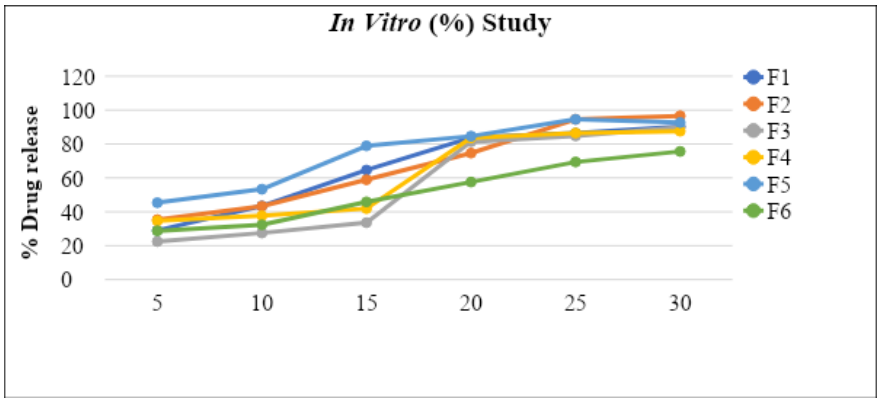

Figure 11- Dissolution profile of nebivolol Hcl immediate Release tablet

Conclusion

It is concluded that immediate release tablet of Nebivolol Hcl was shown satisfactory result by performing Pre-Compression and Post compression Evaluation test. Among all formulation F2 was shown satisfactory result as per ICH guideline and shows quick release within 30 minutes up to 96.62%.

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Reference

[1] LPreethi et al. Formulation and evaluation of immediate release tablets of nebivolol hydrochloride, journal of global trends in pharmaceutical sciences:1790-1796

[2] Srikant pimple et al. Formulation development and evaluation of novel combination s (-) Amlodipine and nebivolol tablets in single unit dosage: 239-243

[3] B. Dharshini Swapna et al. Formulation and evaluation of immediate release tablet of nebivolol hydrochloride, World journal of pharmacy and pharmaceutical sciences: volume 4, issue 1, 687-698.

[4] Rohit S Kulkarni, formulation and evaluation of immediate release tablet of Valsartan, International Journal of pharmaceutical sciences and Research, vol 6, Issue 2 :808-815

[5] D. M Patel et al, Formulation and evaluation of Fast Dissolving Tablets of Nebivolol and Valsartan, International Journal of Pharmaceutical science and Research, vol 11, Issue11:5530-5538

[6] Jaimini M and Rawat s: A Review on immediate Release Drug Delivery System. Research Journal of Pharmaceutical Chemical and Biological Sciences2013: 1721-1730

[7] Ratnaparkhi M., Mohanta G. and Upadhyay L., fast dissolving tablet: A Review. International journal of pharmacy research, 2(1), 2009, 5-12.

[8] Sekharan T.R., Kumar S and Siji R., Formulation and evaluation of mouth dissolving famotidine tablet, International journal of ChemTech Research, 1(4), 2009, 1251-1256.

[9] Kakade S M., Mannur V.S. and Ramani K.B., formulation and evaluation of mouth dissolving tablets

ISSN: 2309-5288 (Print)
ISSN: 2309-6152 (Online)
CODEN: JCLMC4
Journal of Coastal Life Medicine

of losartan potassium, International journal research pharmaceutical sciences, 1(3) , 2010, 290-295.

[10] Vimal Arora, Anil Bhandrai, Gupta V.B, Advances in Direct Compression Technology, Asian journal of pharmaceutics Vol.1 Issue 1, Oct-Dec 2006, 18-21.

[11] Venkadalakshi R., Sasikala C. Swati R., "formulation and evaluation of Granisetron Hydrochloride immediate release Tablets", International journal of Pharmaceutical Sciences, Sep-December 2009, Vol.1,Issue 2, 336-341.

[12] Suresh Bandari, Rajendra Kumar Mittapalli, Ramesh Gannu "immediate release tablets An overview" , Asian journal of pharmaceutics, jan 2008, 2-11.

[13] Shimizu T, sugaya A , Nakano Y, Izutuzu D, Mzukami Y.; formulation study for lansoprazole fast disintegrating tablets, chemical and Pharmaceutical Bulletin, 2003; 51 (10); 1121-1127.

[14] Seong H.J Yourong F, Kinam P, Frosta; a new technology for masking fast melting tablets, Expert opinion on drug delivery,2005; 2(6) ; 1107-1116.

[15] Raju M., Sundaramoorthy K. and Vetrichelvan T. Formulation and In-Vitro Evaluation of Sustained Release Matrix Tablets of Aceclofenac by UsingDifferent Natural Polymers, Research Journal of Pharmaceutical, Biological and Chemical Sciences., 2010, 1(4), 279-291.

[16] Saleh M. Al-Saidan, Yellela S. R. Krishnaiah and Srinivas S. Patro. In-Vitro and InVivo Evaluation of Guar Gum Matrix Tablets for Oral Controlled Release of WaterSoluble Diltiazem Hydrochloride, AAPS Pharm. Sci. Tech., 2005, 6 (1), 1-8.

[17] Amelia Avachat and Vikram Kotwal. Design and Evaluation of Matrix-Based Controlled Release Tablets of Diclofenac Sodium and Chondroitin Sulphate, AAPS Pharm. Sci. Tech., 2007, 8(4), 1-6.

[18] Deepak S. and Rana A.C. Formulation Development of Quetiapine Fumarate SR Matrix Tablets, Pelagia Research Library., 2010, 1(1), 48-57.

[19] Gohel M.C., Parikh R.K. and Padshala M.N. Formulation and Optimization of Directly Compressible Isoniazid Modified Release Matrix Tablet, Indian Journal of Pharmaceutical Sciences., 2007, 69(5), 640-645.

[20] Aulton M.E. Pharmaceutics: The Design and Manufacture of Medicine, 3rd edn., Churchill Livingstone, New York, 2007, 355-359,483-498.

[21] Carstensen J.T. and Rhodes C.T. Drug Stability Principles and Practices, 3rd edn., Marcel Dekker, Inc, New York, 2008, 415-481.

[22] Goodman and Gilman‟s. The Pharmacological Basis of Therapeutics, 10th edn., Harman J.G. and Limbird L.E, New York, 2001, 1349-1359.

[23] Manavalan R. and Ramasamy S. Physical Pharmaceutics, 2nd edn., Vignesh Publisher, Chennai, 2001, 288-299.

[24] Patil U.K., Sourabh Jain and Yadav S.K. Preparation and Evaluation of Sustained Release Matrix Tablet of Furosemide Using Natural Polymers, Research J. Pharm. And Tech., 2008, 374-376.

[25] Raymond C Rowe, Paul J Sheskey and Marian E Quinn. Handbook of Pharmaceutical Excipients, 6th edn., Pharmaceutical Press, London, 2009, 155, 697,772.

[26] Skoog D.A., Holler F.J. and Crouch S.R. Fundamental of Analytical Chemistry, 8th edn., Thomson Asia Pvt. Ltd., Singapore, 2004, 775-781, 811- 819.

[27] Willard H.H., Merritt L.L. and Settle F. A. Instrumental Methods of Analysis, 12th edn., CBS Publishers and Distributors, New Delhi, 2008, 762-766.

[28] Mukesh C. Gohel and Shital H.Bariya. Fabrication of Triple- Layer Matrix Tablets of Venlafaxine Hydrochloride, AAPS Pharmaceutical Sciences Technology., 2009, 10(2), 624-630.

[29] Nikil A Karani and Prashant pingale. Analytical Method Development and Validation of Venlafaxine Hydrochloride in Solid Dosage Form using UV Spectrophotometer, Journal of Pharmacy Research., 2009, 2, 1246-1249.

[30] Vimal D shirvi., Vijayakumar G. and channabasavaraj K.P. Third Order Derivative Spectrophotometric Estimation of Venlafaxine Hydrochloride in Bulk and Pharmaceutical Formulations, International Journal of Pharma Technology and Research., 2010, 2, 700-703.