International Journal of Pharmacy and Analytical Research (IJPAR)
IJPAR |Vol.12 | Issue 4 | Oct - Dec -2023
www.ijpar.com
ISSN: 2320-2831
DOI : https://doi.org/10.61096/ijpar.v12.iss4.2023.557-566

Research

Formulation, development and evaluation of oral disintegrating tablets of lacidipine

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Published on: 17 Oct 2023

Published by:
DrSriram Publications

Abstract

The aim of this study is to formulate and significantly improve the bioavailability and reduce the side effects of oral disintegrating tablets Lacidipine. The precompression blends of Lacidipine were characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio. The precompression blend of all the batches indicates well to fair flowability and compressibility. Oral disintegrating tablets were prepared with various disintegrants like Crospovidone, Croscarmellose sodium, Sodium starch glycolate at different concentration ratios and were compressed into tablets. The formulated tablets were evaluated for various quality control parameters. The tablets were passed all tests. Among all the formulations F4 formulation containing, drug and Crospovidone showed good result that is 98.46% in 30 min. Hence from the dissolution data it was evident that F4 formulation is the better formulation. By conducting further studies like *in vivo* studies, preclinical and clinical studies we can commercialize the product.

Keywords: : Lacidipine, Oral disintegrating Tablets, Crospovidone, Croscarmellose sodium and Sodium starch glycolate.

INTRODUCTION

The oral route of administration is considered as the most widely accepted route because of its convenience of self administration, compactness and easy manufacturing. But the most evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing, leading to patients incompliance particularly in case of pediatric and geriatric patients. but it also applies to people who are ill in bed and to those active working patients who are busy or traveling, especially those who have no access to water. Over a decade, the demand for development of orally disintegrating tablets (ODTs) has enormously increased as it has significant impact on the patient compliance. Orally disintegrating tablets are appreciated by a significant segment of populations particularly who have difficulty in swallowing. It has been reported that Dysphagia.(difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients ,psychiatric patients and patients with nausea, vomiting,

and motion sickness complications. ODTs with good taste and flavor increase the acceptability of bitter drugs by various groups of population.

This dosage form combines the advantages of dry and liquid formulation. Some novel ODT technology allow high drug loading, have an acceptable taste, offer a pleasant mouth felling, leaving minimal residue in the mouth after oral administration.ODT have been investigated for their potential in improving bioavaibility of poorly soluble drug through enhancing the dissolution profile of the drug and hepatic metabolism drugs. Orally disintegrating tablets are also called as orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets,porous tablets, and rapimelts. However, of all the above terms, United States pharmacopoeia (USP) approved these dosageforms as ODTs. Recently, European Pharmacopoeia has used the term orodispersible tablet for tablets that disperses readily and within 3 min in mouth before swallowing.

United States Food and Drug Administration (FDA) defined ODT as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue." The disintegration time for ODTs generally ranges from several seconds to about a minute.

Approaches For Preparation Of ODTs

Various preparation techniques have been developed on the basis of different principles, thus present different properties of ODTs by means of mechanical strength, stability, mouth feel, taste, swallowability, dissolution profile and bioavailability. Some of those technologies are patented. Basic pharmaceutical processes to manufacture ODTs are explained as follows:

Spray drying

Spray drying methods are used to a great extent in pharmaceutical and biochemical procedures. Spray drying provides a rapid and economically efficient way to eliminate solvents and produces highly porous and fine powders. The formulations are compounded by hydrolyzed and non hydrolyzed gelatins as supporting agents, mannitol as bulking agent, croscarmellose sodium or sodium starch glycolate as disintegrating agent. An acidic material (e.g., citric acid) or alkali material (e.g., sodium bicarbonate) is used to improve disintegration and dissolution behaviour. Tablets prepared by the compression of spray dried powder, when immersed in an aqueous medium, showed a disintegration time of 20s.

Sublimation

Compressed tablet which contains highly water-soluble components can show slo dissolution behaviour, due to the low porosity of the tablets that reduces water penetration into the matrix. By conventional methods, volatile materials are compressed into tablets, these volatile materials can be removed by sublimation, which results in extremely porous structures. The volatile materials which can be used are ammonium carbonate, urea, ammonium bicarbonate, camphor and hexa methylene tetramine. In a few cases, thymol, menthol, camphor, an organic acid such as adipic acid and fatty acid such as arachidic acid, myristic acid, capric acid, and palmitic acid were used as the volatile materials and the sublimation temperature ranged from 40 ºC to 60 ºC. The disintegration time in the oral cavity was found to be about 25s**.**

Freeze drying

Lyophilization process involves removal of solvents from a frozen drug solution or a suspension containing structure-forming excipients. The tablets formed by this process are usually very light and have highly porous structures that allow, rapid dissolution or disintegration. Lyophilization is done at very low temperature to eliminate the adverse thermal effects that may alter drug stability during processing. The freeze dried dosage form have relatively few stability concerns during its shelf life. The drying process may give rise to the glassy amorphous structure of excipients and drug substance.

Molding

Molded tablets are made up of watersoluble ingredients. The powder mixture is sprinkled with a solvent (usually water or ethanol). The mixture is molded into tablets under pressure. Applied pressure should be lower than those used in conventional tablet compression. This process is also known as compression molding. Air drying can be used to remove the solvent. Due to lower pressure; a highly porous structure is created, that enhances the dissolution. The powder blend should be passed through a very fine screen, to improve the dissolution rate. Molded tablets disintegrate more rapidly and provide improved taste because of their highly water-soluble, sugar components. However, molded tablets generally do not have high mechanical strength. The chances of breakage of the molded tablets during tablet handling and opening of blister pockets, is very high. If the hardness enhancing agents are used in the formulation, decrease in disintegration rate is observed. Mechanical strength and good disintegration of the tablets can be improved by using non-

conventional equipment and by using multistep processes.

Mass extrusion

The mass extrusion technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol and methanol. Expulsion of softened mass through the extruder or syringe is carried out, to get a cylinder of the product which is then cut into even segments using a heated blade to form tablets .

Direct compression

Direct compression is the easiest and costeffective tablet manufacturing process. This method can be applied to manufacture ODT by selecting appropriate combinations of excipients, which can provide fast disintegration and optimum physical resistance. Sugar-based excipients are widely used as bulking agents because of their aqueous solubility, sweetness pleasing mouth feel, and good taste masking. Tablets obtained by conventional compression method are less friable, but disintegrate more slowly. The compression method, with or without wet granulation, is a convenient and cost effective way to prepare tablets with sufficient structural integrity .

MATERIALS AND METHODS

Lacidipine Procured From Themis Laboratories PVT LTD, Mumbai (India). Provided by SURA LABS, Dilsukhnagar, Hyderabad. Chitosan fromPanchi Chemicals Pvt Ltd, Mumbai, Carbopol from Alkem Labs Pvt, Ltd, Mumbai, Lactose from Sd fine Chem.Ltd. Mumbai, Magnesium stearate from SD Fine chemicals, Mumbai, Talc from Qualigens fine chemicals, Mumbai, Aspartame from SD Fine chemicals, Mumbai.

Buffer preparation

Preparation of 0.2 M Potassium dihydrogen orthophosphate solution: Accurately weighed 27.128 gm of monobasic potassium dihydrogen orthophosphate was dissolved in 1000 ml of distilled water and mixed.

Preparation of 0.2 M sodium hydroxide solution: Accurately weighed 8 gm of sodium hydroxide pellets were dissolved in 1000 mL of distilled water and mixed.

Preparation of pH 6.8 phosphate buffer: Accurately measured 250 mL of 0.2 M potassium dihydrogen orthophosphate and 112.5 mL of 0.2 M NaOH was taken into the 1000 mL volumetric flask. Volume was made up to 1000 mL with distilled water.

Analytical method development for Lacidipine

Determination of absorption maxima

A spectrum of the working standards was obtained by scanning from 200-400 nm against the reagent blank to fix absorption maxima. The λmax was found to be 242 nm. Hence all further investigations were carried out at the same wavelength.

Construction of standard graph

100 mg of Lacidipine was dissolved in 100 mL of pH 6.8 phosphate buffer to give a concentration in 1mg/mL (1000µg/mL) 1 ml was taken and diluted to 100 ml with pH 6.8 phosphate buffer to give a concentration of 0.01 mg/ml (10µg/ml). From this stock solution aliquots of 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml, 1 ml, were pipette out in 10 ml volumetric flask and volume was made up to the mark with pH 6.8 phosphate buffer to produce concentration of 2,4,6,8 and 10µg/ml respectively. The absorbance of each concentration was measured at respective (λmax) i.e., 242nm.

Formulation development

Drug and different concentrations of super disintegrants (Crospovidone, Croscarmellose sodium and Sodium starch glycolate) and required ingredients were accurately weighed and passed through a 40-mesh screen to get uniform size particles and mixed in a glass motor for 15 min.

- The obtained blend was lubricated with magnesium stearate and glidant (Talc) was added and mixing was continued for further 5 min.
- The resultant mixture was directly compressed into tablets by using punch of rotary tablet compression machine, Compression force was kept constant for all formulations.

Table 1: Formulation table showing various compositions

INGREDIENTS	FORMULATION CODE											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Lacidipine	4	4	4	4	4	4	4	4	4	4	4	4
Crospovidone	10	20	30	40	-	-	-	-	-	-	-	-
Croscarmellose sodium	-	-	-	-	10	20	30	40	-	-	-	-
Sodium starch glycolate	-	-	-	-	-	-	-	-	10	20	30	40
Colloidal silicon dioxide	2	2	2	2	2	2	2	2	2	2	2	2
Magnesium stearate	5	5	5	5	5	5	5	5	5	5	5	5
Talc	4	4	4	4	4	4	4	4	4	4	4	4
Mannitol	5	5	5	5	5	5	5	5	5	5	5	5
MCC	120	110	100	90	120	110	100	90	120	110	100	90
Total weight	150	150	150	150	150	150	150	150	150	150	150	150

RESULT AND DISCUSSION

Solubility Studies

Preparation of calibration curve of Lacidipine

The regression coefficient was found to be 0.999 which indicates a linearity with an equation of y=0.057 x-0.003. Hence Beer-Lambert's law was obeyed.

Table 2: Calibration curve data of Lacidipine in pH 6.8 phosphate buffer

Concentration	Absorbance
0	0
2	0.119
4	0.238
6	0.347
8	0.461
10	0.574

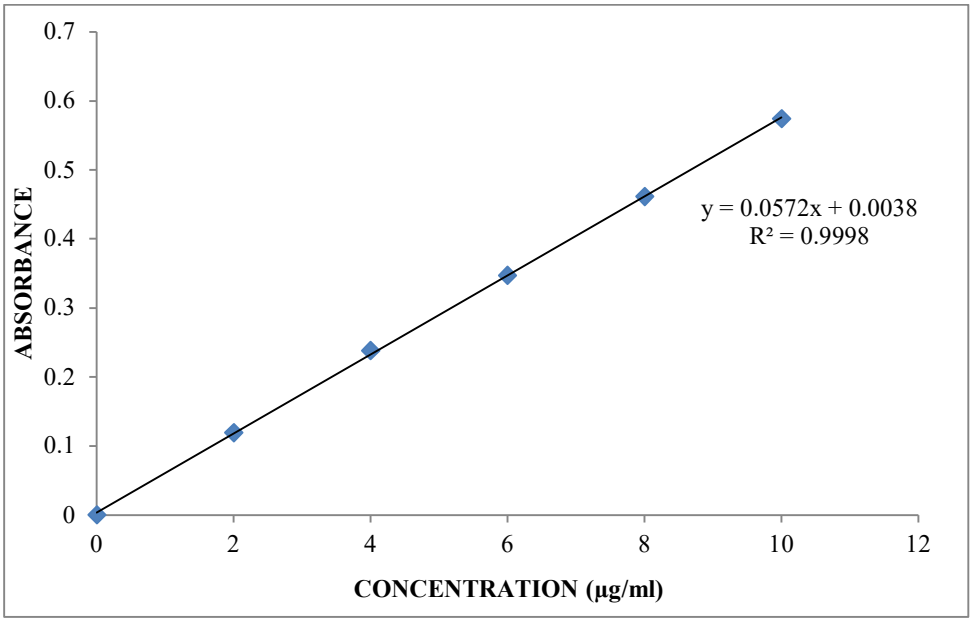

Fig 1: Calibration curve data of Lacidipine in pH 6.8 phosphate buffer

Evaluation of pre-compresion parameters of powder blend

Table 3: Evaluation of pre-compression parameters of powder blend

Formulation code	Angle of repose	Bulk density(gm/mL)	Tapped density (gm/mL)	Carr's index(%)	Hausner's ratio
F1	35.13±0.032	0.4236±0.0026	0.4854±0.0018	12.73±0.0494	1.14±0.0014
F2	35.15±0.041	0.4230±0.0020	0.4766±0.0033	11.23±0.1272	1.12±0.0035
F3	29.24±0.008	0.4127±0.0180	0.4821±0.0029	14.36±0.7566	1.16±0.0000
F4	27.47±0.027	0.4227±0.0038	0.5231±0.0253	19.19±0.0565	1.23±0.0071
F5	35.12±0.019	0.3823±0.0032	0.4852±0.0044	20.01±0.0848	1.26±0.0000
F6	34.99±0.003	0.3910±0.0014	0.4650±0.0036	15.90±0.3040	1.16±0.0070
F7	33.86±0.002	0.2896±0.0014	0.3449±0.0013	16.04±0.3676	1.18±0.0424
F8	35.23±0.001	0.3100±0.0035	0.3655±0.0031	15.19±0.2969	1.17±0.0070
F9	32.61±0.001	0.3925±0.0026	0.4614±0.0028	14.93±0.9545	1.16±0.0070
F10	31.60±0.017	0.4082±0.0071	0.4808±0.0020	15.09±1.4495	1.17±0.0141
F11	34.21±0.006	0.3683±0.0009	0.4473±0.0002	17.66±0.0212	1.21±0.0212
F12	34.75±0.003	0.4214±0.0068	0.5245±0.0013	19.64±0.5020	1.24±0.0070

- For each formulation blend of drug and excipients were prepared and evaluated for various pre compression parameters described earlier in methodology chapter.
- The bulk density of all formulations was found in the range of 0.2896±0.0014 - 0.4236±0.0026 and tapped density was in the range of 0.3449±0.0013 - 0.5245±0.0013 The Carr's index and Hausner's ratio was calculated from tapped density and bulk density.

Evaluations of post compression parameters of lacidipine odts

Table 4: Evaluation of post compression parameters of Lacidipine oral disintegrating tablets

Formulation codes	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)	*In vitro* disintegration Time (Sec)
F1	148.5	4.2	0.36	3.69	98.16	49
F2	149.3	4.9	0.24	3.48	97.62	36
F3	147.8	4.6	0.59	3.15	99.35	31
F4	145.6	4.1	0.37	3.75	96.28	15
F5	149.2	4.7	0.49	3.61	97.19	31
F6	148.8	4.3	0.36	3.95	99.25	28
F7	147.2	4.2	0.75	3.47	99.61	20
F8	149.2	4.0	0.48	3.64	98.18	18
F9	146.7	4.8	0.57	3.18	97.29	23
F10	148.6	4.6	0.64	3.10	98.66	49
F11	149.3	4.1	0.56	3.69	99.45	56
F12	148.9	4.9	0.24	3.73	98.14	37

Weight variation and Thickness

All the formulations were evaluated for uniformity of weight using electronic weighing balance and the results are shown above. The average tablet weights of all the formulations were noted down.

Hardness and friability

All the ODT formulations were evaluated for their hardness using Monsanto hardness tester and the results are shown above. The average hardness for all formulations was found to be between (4.0 - 4.9) kg/cm^2 which was found to be acceptable. Friability was determined to evaluate the ability of the tablets to with stand the abrasion during packing, handling and transporting. All the ODT formulations were evaluated for their percentage friability using Roche friabilator and the results are shown above. The average percentage friability for all the formulations was between 0.24 - 0.75 which was found to be within the limit.

Drug content

All formulations were evaluated for drug content according to the procedure described in methodology section and the results were shown above. The assay values for all formulations were found to be in the range of (96.28 – 99.61%). According to IP standards the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all the ODT formulation comply with the standards given in IP.

***In vitro* disintegration time:** *In vitro* disintegration studies showed from 15-56 sec. The F4 formulation showed *in vitro* disintegration time i.e. 15 seconds.

***In vitro* drug release syudies of lacidipine**

Table 4: Dissolution data of Lacidipine

Time (Min)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0	0	0	0	0	0	0
5	34.62	36.97	36.82	43.18	46.16	35.26	31.68	29.14	41.46	44.06	51.84	47.62
10	46.86	47.15	48.58	56.29	53.78	43.61	47.84	37.51	46.88	52.09	57.32	53.18
15	55.23	56.60	56.34	63.15	69.62	56.27	56.88	49.28	57.52	62.75	68.02	61.40
20	67.19	67.58	69.21	72.94	77.43	59.19	63.16	57.61	63.03	73.48	76.18	75.14
25	72.17	78.12	75.14	89.67	83.25	66.42	72.72	66.25	84.13	89.45	84.38	81.26
30	79.27	83.33	87.72	98.46	96.53	83.65	76.32	72.14	92.38	97.73	90.03	89.11

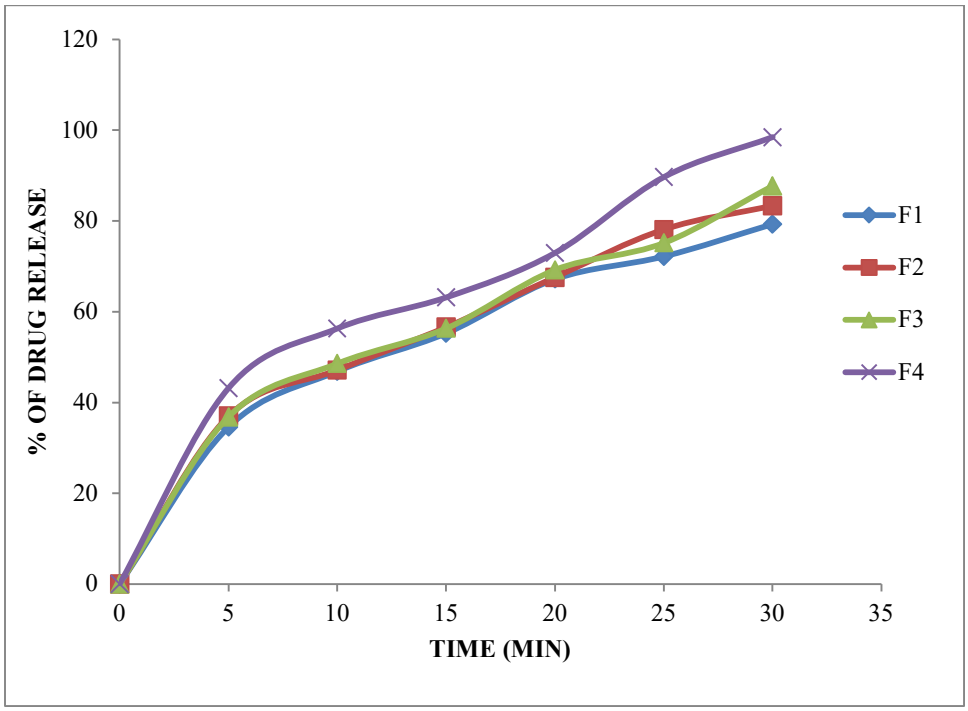

Fig 2: Dissolution profile of formulations F1,F2,F3,F4

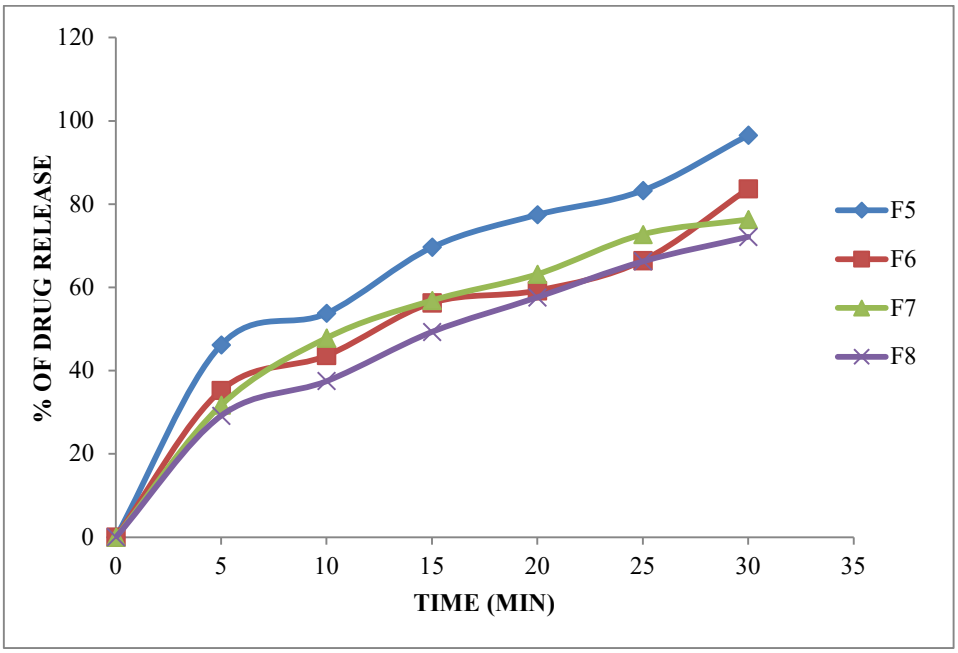

Fig 3: Dissolution profile of formulations F5,F6,F7, F8

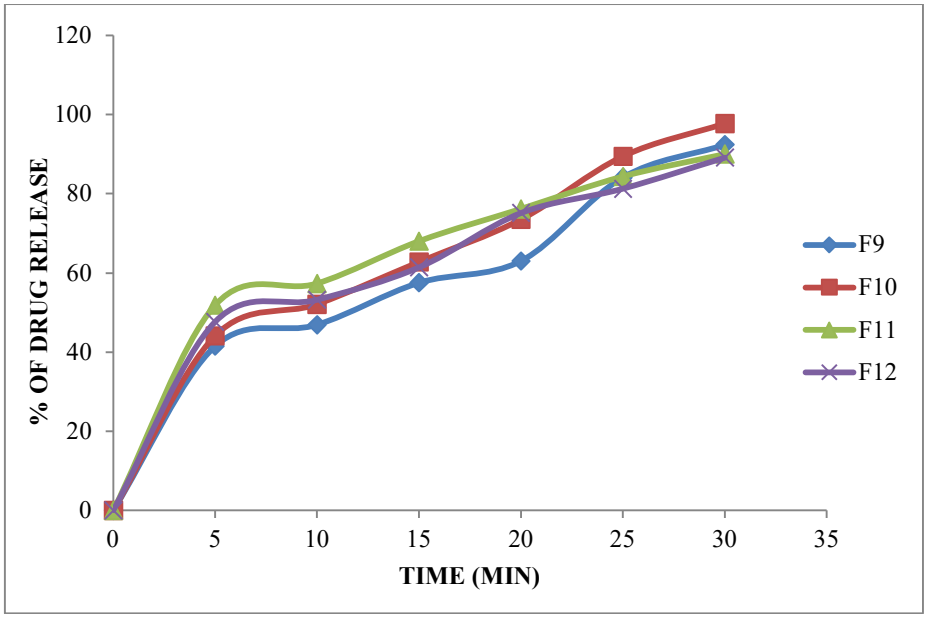

Fig 4: Dissolution profile of formulations F9,F10,F11,F12

From the table it was evident that the formulation prepared with Crospovidone were showed good drug release i.e., F4 formulation (98.46%) in higher concentration of Blend i.e. 40 mg. Formulations prepared with Croscarmellose sodium showed good drug release i.e., 96.53 % (F5 formulation) in 10 mg concentration. When increase in the concentration of Croscarmellose sodium drug release unable to retarded. Formulations prepared with Sodium starch glycolate showed maximum drug release i.e., 97.73 % (F10 formulation) at 30 min in 20 mg of blend.

Among all formulations F4 considered as optimized formulation which showed maximum drug release at 30 min i.e., 98.46 %. Crospovidone showed good release when compared to Sodium starch glycolate. Finally concluded that F4 formulation contains Crospovidone was optimized formulation.

FTIR results

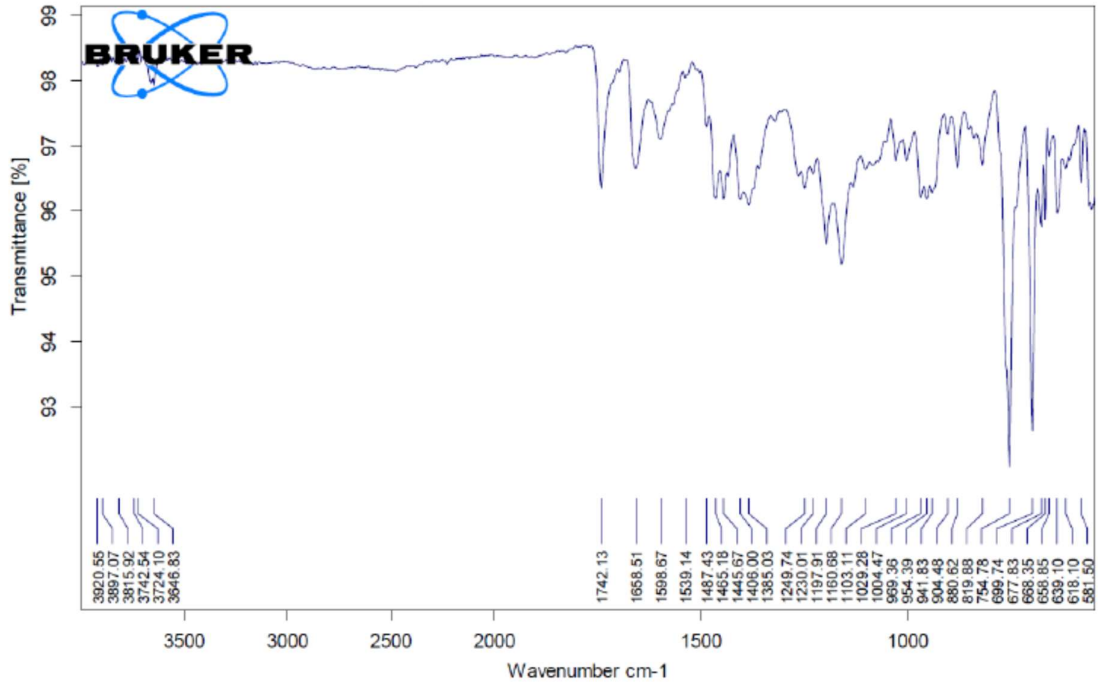

Fig : FTIR of Lacidipine Pure Drug

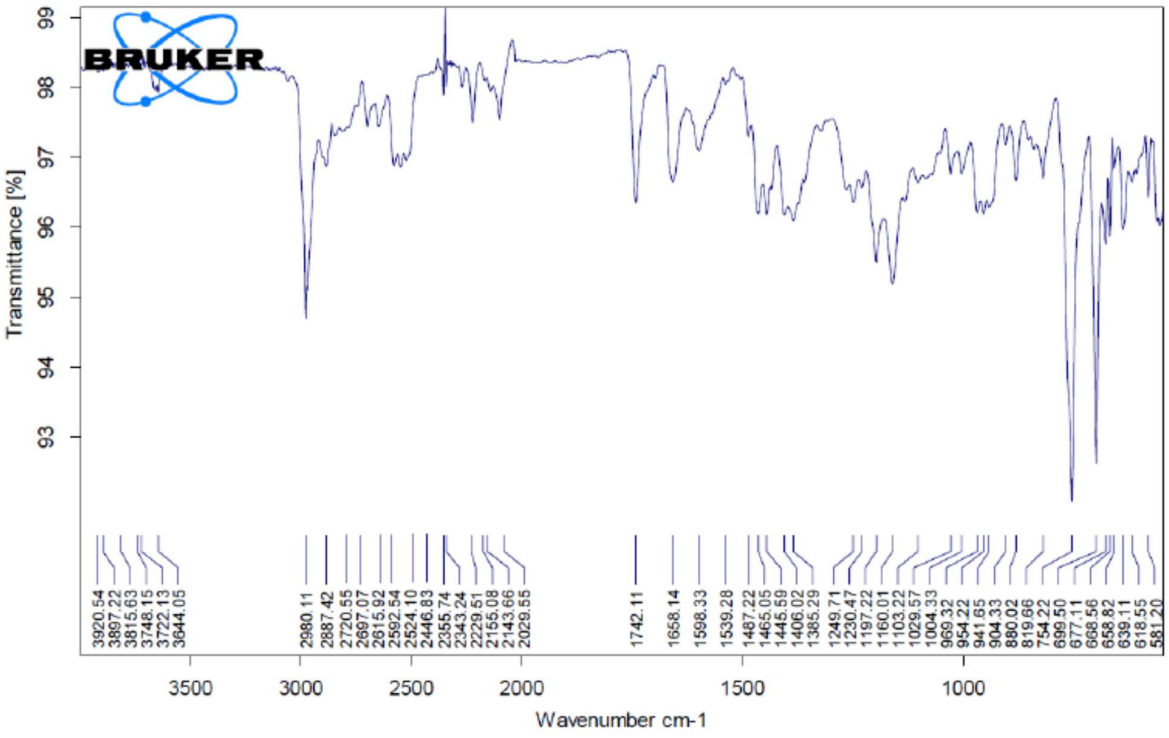

Fig : FTIR of Lacidipine optimized formulation

From the above studies it was found that there was no shifting in the major peaks which indicated that there were no significant interactions occurred between the Lacidipine and excipients used in the preparation of

different Lacidipine Oral disintegrating tablets formulations. Therefore the drug and excipients are compatible to form stable

Formulations under study The FTIR spectra of Lacidipine and physical mixture used for optimized formulation were obtained and these are depicted in above figures. From the FTIR data it was evident that the drug and excipients does not have any interactions. Hence they were compatible.

CONCLUSION

The standard curve of Lacidipine was obtained and good correlation was obtained with R^2 value of 0.999. The medium selected was pH 6.8 phosphate buffer. Lacidipine was mixed with various proportions of excipients showed no colour change at the end of 2 months, proving no drug-excipient interactions. The pre compression blend of Lacidipine oral disintegrating tablets using super disintegrants were characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio. The precompression blend of all batches indicating good to fair flowability and compressibility. Oral disintegrating tablets were prepared with various concentrations of disintegrants, and were compressed into tablets. The formulated tablets were evaluated for various quality control parameters. The tablets were passed all the tests. The formulations (F1-F4) prepared with Crospovidone disintegrants showed drug release in increasing order. The formulation (F4) containing drug and Crospovidone showed good drug release (98.46% at 30min) at 40 mg concentration. Among all the formulations F4 formulation containing drug and Crospovidone (40 mg concentration) showed maximum and good result that is 98.46% drug release in 30 min. Hence from dissolution data it was evident that F4 formulation is the better formulation.

REFERENCES

1. Velmurugan S and Sundar Vinushitha. Oral Disintegrating Tablets: An Overview. International Journal of Chemical and Pharmaceutical Sciences 2010, Dec., Vol.1 (2).
2. Seager H. Drug-delivery products and the Zydis fast-dissolving dosage form. Journal of Pharmacy and Pharmacology. 1998; 50(4):375-82.
3. Lindgren S, Janzon L. Dysphagia; Prevalence of swallowing complaints and clinical findings. Medical clinics of North America., 1993; 77: 3-5.
4. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets: Developments, technologies, taste-masking and clinical studies. Critical Review in Therapeutic Drug Carrier System. 2004;21:433-76.
5. Brown D. Orally Disintegrating TabletsTaste over Speed. Drug Delivery Technology. 2003; 3:58-61.
6. Kumaresan C, Orally Disintegrating Tablet - Rapid Disintegration, Sweet Taste, And Target Release Profile, pharmainfo.net sep9 2008.
7. Reddy L. H, Ghosh B, and Rajneesh. Fast dissolving drug delivery systems: a review of the literature. Indian Journal of Pharmaceutical Science. 2002; 64(4): 331-336.
8. Seager H. Drug-deliver products and the zydis fast-dissolving dosage form. Journal of Pharmacy and Pharmacology. 1998;50: 375-382.
9. Parijat Pandey, Mandeep Dahiya. Oral Disintegrating Tablets: A Review. International Journal of Pharma Research & Review, Jan 2016;5(1):50-62.
10. .Seager H. Drug delivery products and the zydis fast dissolving dosage form. Journal of Pharmacy and Pharmacology 1998;50(4): 375-382
11. Habib W, Khankari R, Hontz J. Fast dissolving drug delivery system. Critical Reviews in Therapeutic Drug Carrier Systems 2000; 17(1):61-72.
12. Gafiţanu E, Dumistracel I, Antochi S. Formulations and bioavailability of propyphenazone in lyophilized tablets. Revista Medico-chirurgicala a Societatii De Medici Si Naturalisti Din Iasi 1991;95(1- 2):127-128.
13. Bharadwaj S, Jain V, Sharma S, Jat RC, Jain S. Orally Disintegrating Tablets: A Review. Drug Invent Today 2010;2(1):81-88.
14. Vani R, Rasheed A. Formulation and evaluation of hydrochlorothiazide and ramipril mouth dissolving tablet using different superdisintegrants. International Journal of Pharma Sciences and Research 2014;5(1):207-212.
15. Parkash V, Maan S, Deepika, Yadav SK, Hemlata, Jogpal V. Fast disintegrating tablets: Opportunity in drug delivery system. Journal of Advanced Pharmaceutical Technology and Research 2011;2(4):223-235.
16. Ashish P, Harsoliya MS, Pathan JK, Shruti S. A review - Formulation of mouth dissolving tablet. International Journal of Pharmacology and Clinical Sciences 2011;1(1):1-8.
17. Shukla S, Mishra DK, Jain DK. New insights in the field of fast dissolving tablets. Journal of Hormonized Research in Pharmacy 2015;4 (3):213-226.
18. Bera A, Mukherjee A. A detailed study of mouth dissolving drug delivery system. Acta Chimica Pharmceutica and Indica 2013;3(1): 65-93.

19. Reddy AM, Babu PS, Harshita B, Sravya R. Conventional and patented technologies in oral dispersible tablets: a review. Journal of Chemical and Pharmaceutical Sciences 2013; 6(4):286-292.
20. Siddiqui MN, Garg G, Sharma PK. Fast dissolving tablets: preparation, characterization an evaluation: an overview. International Journal of Pharmaceutical Sciences Review and Research 2010;4(2):87- 96.