WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.045
Volume 3, Issue 10, 1292-1304. Research Article ISSN 2277–7105

FORMULATION AND EVALUATION OF FAST DISINTEGRATING TABLETS OF LAMIVUDINE USING OCIMUM BASILICUM SEED MUCILAGE AS SUPERDISINTEGRANT

Dr. M. Sunitha Reddy*[1], Tangella Srividyalalitha[2]

Centre for Pharmaceutical Sciences, Institute of Science and Technology, Jawaharlal Nehru Technological University, Kukatpally, Hyderabad, Telangana, India.

Article Received on
08 October 2014,

Revised on 02 Nov 2014,
Accepted on 26 Nov 2014

***Correspondence for Author**
Dr. M. Sunitha Reddy
Centre for Pharmaceutical Sciences, Institute of Science and Technology, Jawaharlal Nehru Technological University, Kukatpally, Hyderabad, Telangana, India.

ABSRACT

The objective of current study involves the formulation and evaluation of fast disintegrating tablets of Lamivudine using natural superdisintegrant obtained from pericarp of Ocimum basilicum seed. Pre compression properties of tablet blend shows that the blend has good flow properties. Six formulations were prepared and post compression properties shows that the formulation F2 was the best formulation as it disintegrated within 22.79±0.01 seconds, drug release was 99.4±0.41% at 10minutes. It was subjected to accelerated stability studies at RH 75% and 40^0 C for a period of one month. The formulation was found to be stable.

KEYWORDS: Fast disintegrating tablet, Lamivudine, Natural superdisintegrant, Ocimum basilicum seed mucilage.

INTRODUCTION

Natural excipients are in demand over synthetic excipients because of their renewable source, biocompatibility, biodegradability, low cost and ecofriendly nature. [1] Ocimum basilicum plant have been used in traditional medicine due to its medicinal properties like antibacterial, antifungal, antispasmodic, carminative, diaphoretic, digestive, emmenagogue, expectorant, stimulant, stomachic. The plant is generally used in treatments of problems concerning digestion and nervous system. [2] Lamivudine is an anti retroviral drug and also used for the treatment of hepatitis B. It is used by the pregnant women to prevent mother to child transmission of HIV. It is also used for treatment of HIV in children.[3] Present study involves

the formulation of Lamivudine fast disintegrating tablets using the mucilage obtained from the seeds of Ocimum basilicum.

MATERIALS AND METHODS

Ocimum basilicum seeds were obtained from Ayurvedic pharmacy, Lamivudine was a gift sample from Mylan Laboratories, Hyderabad, Mannitol, Talc, Magnesium stearate, Mint flavor were purchased from Merc.

Isolation of Mucilage from Ocimum basilicum seeds

Basil seeds were rinsed with water to remove foreign particles. Seeds were soaked in water (seed: water= 1:10) for 20 minutes. The swollen seeds subjected to high agitation using homogenizer at 1500 rpm to separate gel layer from seeds. The separated gel layer was passed through muslin cloth to remove unwanted particles and then precipitated using acetone. The precipitate was washed with ethanol and dried in Hot air Oven at 40^0 C. The dried mucilage was powdered and stored in airtight containers. [4, 5, 6, and 7]

Characterization of Ocimum basilicum seed mucilage

The mucilage characterized for Organoleptic evaluation, morphology, phytochemical characteristics, and flow properties.

Organoleptic evaluation

It was done to evaluate color, odor, taste of the Isolated mucilage [8].

Morphology

It was determined by X- ray diffraction, Scanning electron microscopy. X- Ray diffraction: A Powder XRD (PXRD) pattern of mucilage was recorded using X-ray diffractometer. [9]

Scanning Electron Microscopy: The surface topography, morphology was determined by Scanning Electron Microscopy. [10]

Physicochemical Evaluation

These parameters are useful for the identification of purity of the compound. In this the Ocimum basilicum seed mucilage was evaluated for total ash, water soluble ash, acid insoluble ash and swelling index, alcohol soluble extractive, ether soluble extractive, loss on drying. [11]

Phytochemical Evaluation

1%w/v solution of extract was prepared with distilled water. The extract was evaluated for carbohydrates and gums, mucilages. [12]

Flow properties

Flow properties were determined by angle of repose, Hausner's ratio, Carr's index.

P^H: P^H of 1%w/v solution of Ocimum basilicum seed mucilage was determined using P^H meter.

Preformulation Studies

Solubility studies: Solvents like distilled water, ethanol, 0.1N HCl, pH 6.8 phosphate buffer were used for the solubility determination of Lamivudine.

Preparation of 0.1N HCl: 10ml of 36% w/v HCl is diluted to 1000ml using distilled water. Preparation of pH 6.8 phosphate buffer: Dissolve 28.80g of disodium hydrogen phosphate and 11.45g of potassium dihydrogen phosphate in sufficient water to produce 1000ml.

Drug, superdisintegrant Compatibility studies

FTIR spectroscopy was used for compatibility study. Drug and Ocimum basilicum seed mucilage were mixed in 1:1 ratio and kept at 40^0C for 15 days. Drug and excipient mixture was taken and added with Kbr (1:10) ratio and made a pellet. Spectrum of the drug, excipient mixture was scanned using FTIR spectrophotometer in a range 4000-400cm^{-1} [13].

Formulation of Fast Disintegrating Tablets of Lamivudine

Six formulations of Lamivudine FDT were prepared using Ocimum basilicum seed mucilage as superdisintegrant, microcrystalline cellulose as filler, Mannitol as a sweetening agent, peppermint as a flavoring agent, Talc as glidant and Magnesium stearate as lubricant. The drug and excipients were passed through sieve no 60. The tablets were punched using 12.5mm punch using a rotary tablet press [14, 15].

Table 1: Formulation of Fast disintegrating tablets of Lamivudine.

Ingredient	F1 (mg)	F2(mg)	F3(mg)	F4(mg)	F5(mg)	F6(mg)
Lamivudine	150	150	150	150	150	150
Microcrystalline cellulose	97.5	97.5	97.5	97.5	97.5	97.5
Superdisintegrant-Ocimum basilicum seed mucilage	32.5	65	97.5	130	162.5	195
Talc	5	5	5	5	5	5
Magnesium stearate	5	5	5	5	5	5
Mint flavor	1	1	1	1	1	1

Mannitol	359	326.5	294	261.5	229	196.5
Total weight	650	650	650	650	650	650

Evaluation Tests

The tablet blend is evaluated for Angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio. [11]

All batches of tablets were evaluated for the different parameters like thickness, diameter, hardness, weight variation, friability, drug content, wetting time, water absorption ratio, and in-vitro disintegration, in- vitro drug dissolution.

Drug content or content uniformity test

30 tablets were taken and assay was done for 10 tablets.

Assay: Tablets were accurately weighed and powdered. The powder equivalent to 10mg was taken and it was dissolved in 10ml pH 6.8 buffer and made up to 100ml with buffer. 1ml of the stock is further diluted to 10ml with the buffer. Absorbance was measured using UV-Visible spectrophotometer at 270.80nm.

Wetting time: A piece of tissue paper folded twice was kept on a Petri plate. To that 6ml of purified water was added. A tablet was placed carefully on the tissue paper. The time required for the water to reach the upper surface of the tablet was recorded as the wetting time. [13]

Water absorption ratio [13]

Place 6ml of water in a Petri dish and place double folded tissue paper into it. A pre weighed tablet was placed onto a tissue paper. After complete absorption the tablet reweighed and water absorption rate was calculated by

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

Where W_b = weight of the tablet before water absorption

W_a = weight of the tablet after water absorption

In vitro drug disintegration test

It was done by the Petri dish method. In this a Petri dish having a 10cm diameter was taken and 10ml of pH 6.8 phosphate buffer was placed into it and a tablet was placed in the centre of Petri dish. The time required for the complete disintegration tablet was noted. [16]

In vitro drug dissolution test

It was performed using USP II dissolution apparatus. Six tablets were placed in six bowls containing 900ml pH 6.8 phosphate buffer. The paddles are allowed to rotate at 50rpm and at a temperature of 37+0.5. The samples are withdrawn at different time intervals and an equivalent amount of dissolution medium is reintroduced. The samples are diluted and absorbance was noted at 270.80nm using a UV Visible spectrophotometer and percentage of drug release was calculated. [11]

Stability studies

Stability of a drug has been defined as the ability of a particular formulation, in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light and enables recommended storage conditions, re test periods and shelf life to be established. In the present study, the FDT are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies 40 ± 2^0C, RH 75%±5%. The tablets were withdrawn after period of one month and analyzed for physical characterization (visual defects, hardness, friability, disintegration, dissolution etc) and drug content. [17]

RESULTS AND DISCUSSION

Characterization of Ocimum basilicum seed mucilage

Table 2: Characterization of Ocimum basilicum seed mucilage.

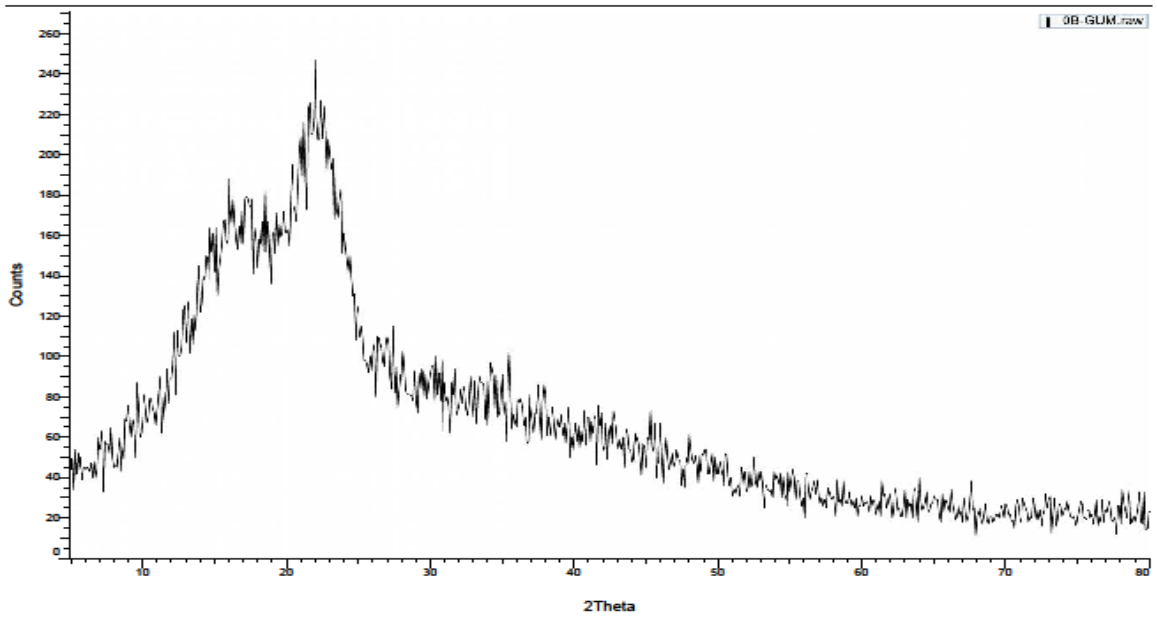
S.NO.	TEST	OBSERVATION
1.	Color	Brownish yellow
2.	Odor	Characteristic
3.	Physico chemical evaluation	
	Total ash	3.465%w/w
	Water soluble ash	1.4%w/w
	Acid insoluble ash	0.2%w/w
	Ethanol soluble extractive	4%w/w
	Ether soluble extractive	4.2%w/w
	Loss on drying	2%
	Swelling index	1712.5

4.	Phytochemical Evaluation	
	Test for carbohydrates	
	Molisch Test: To the test solution add few drops of alcoholic α- naphthol, and then add few drops of concentrated sulphuric acid through sides of test tube.	Purple to violet color ring appeared at the junction
	Gums and Mucilages a) Treat the test solution with Ruthenium red solution. b) The extract is treated with 25ml of absolute alcohol, and filtered.	Pink color was observed Swelling of extract was observed
5.	Flow properties	
	Angle of repose	$19^{0}.42$”
	Bulk density	0.732g/CC
	Tapped density	0.839g/CC
	Compressibility Index	12.75%
	Hausner’s ratio	1.14
6.	P^{H}	7.8

Morphology of Ocimum basilicum seed mucilage powder

X-Ray Diffraction

XRD of Ocimum basilicum seed mucilage



X- ray diffraction shows that the Ocimum basilicum seed mucilage is amorphous.

Scanning Electron Microscopy.

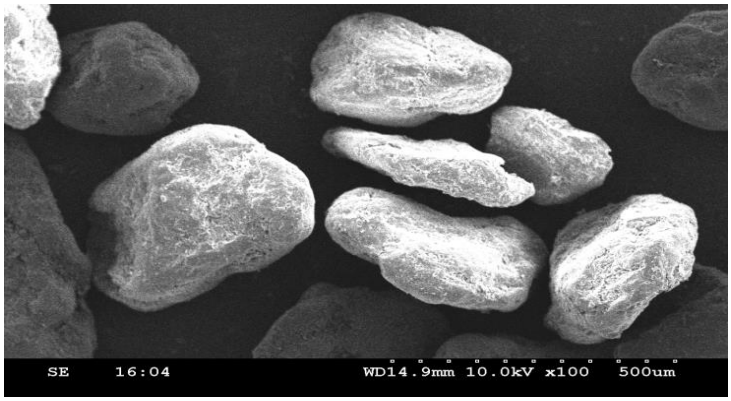


Fig 1: SEM of Ocimum basilicum seed mucilage.

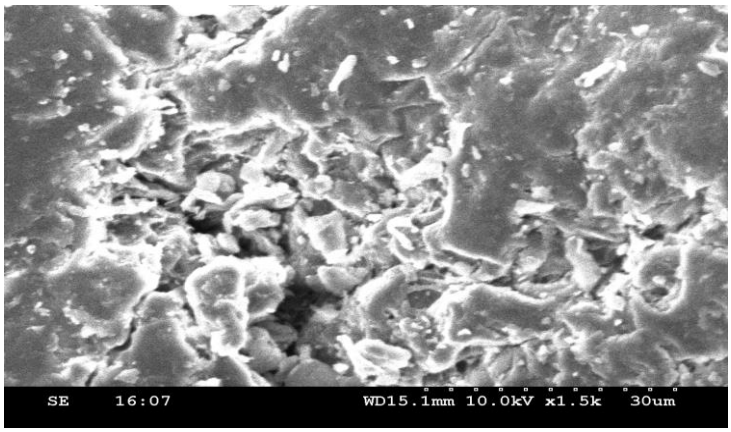


Fig 2: SEM surface view of Ocimum basilicum seed mucilage.

Scanning electron microscopy was done in IICT using SEM Hitachi- S520. SEM photographs shows that the mucilage powder is irregular in shape and has porous nature.

Preformulation Studies

Solubility Studies: Lamivudine is soluble in water, 0.1N HCl, pH 6.8 phosphate buffer, slightly soluble in ethanol.

Drug Excipient compatibility Study

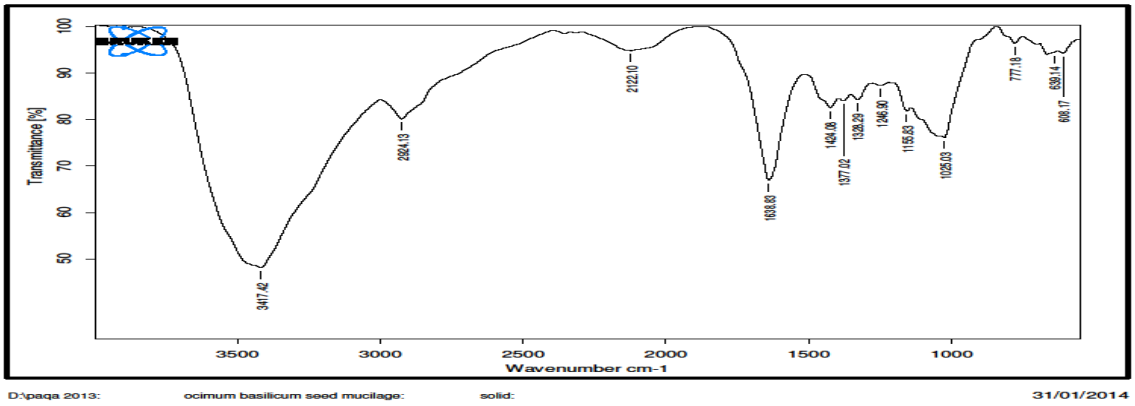


Fig. 3 FTIR of Ocimum basilicum seed mucilage.

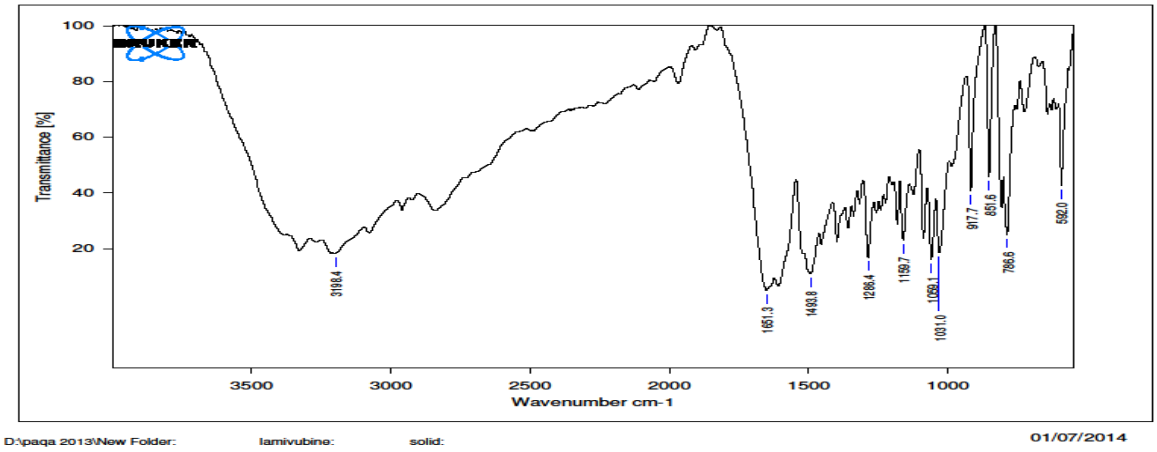


Fig 4: FTIR spectrum of Lamivudine.

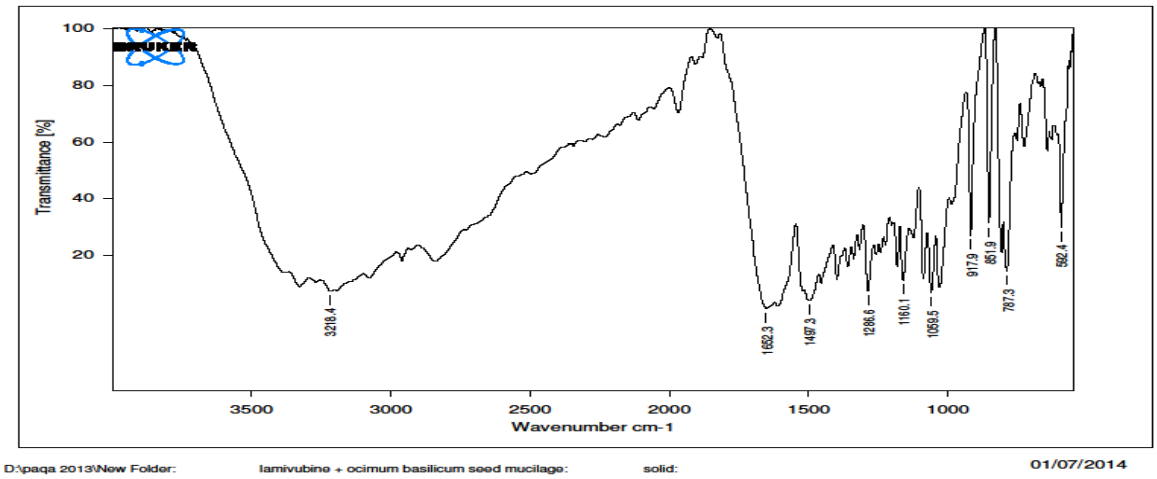


Fig 5: FTIR spectrum of Lamivudine + Ocimum basilicum seed mucilage.

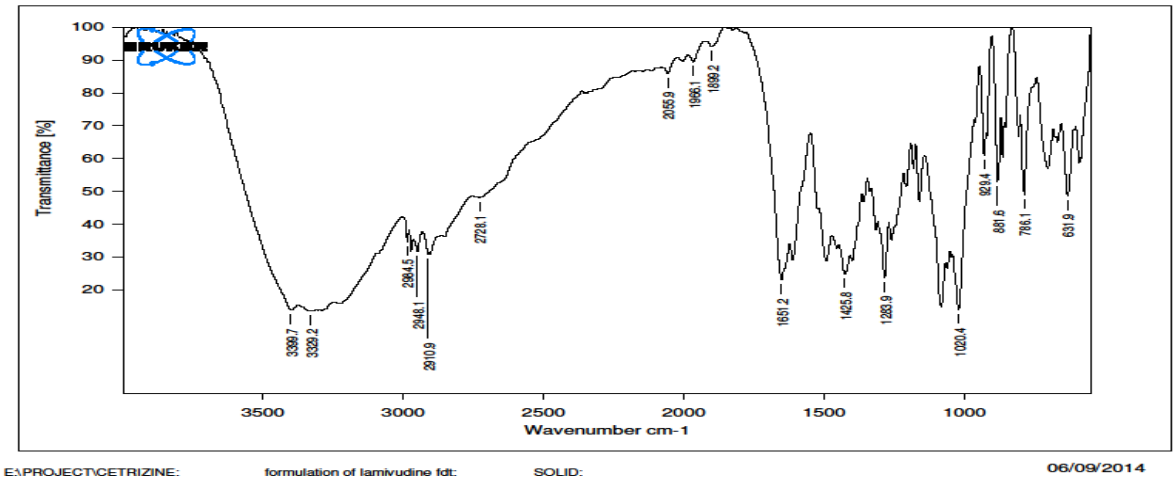


Fig 6: FTIR spectrum of Lamivudine FDT formulation.

All the principle peaks of Lamivudine were retained in FTIR spectrum of 1:1 physical mixture of Lamivudine and Ocimum basilicum seed mucilage. Hence there was no interaction between Lamivudine and Ocimum basilicum seed mucilage. All the principle peaks of Lamivudine were retained in FTIR spectrum of Formulation of Lamivudine. Hence drug and excipients are compatible.

Pre compression Parameters

Table 3 Pre compression parameters.

Formulation	Angle of repose (Ɵ)	Bulk density(g/cc)	Tapped density(g/cc)	Carr's index	Hausner's ratio
F1	31.42^0	0.37	0.46	19.56%	1.24
F2	30.33^0	0.45	0.53	15.09%	1.17
F3	29.6^0	0.39	0.45	13.33%	1.15
F4	29.12^0	0.39	0.44	11.36%	1.12
F5	28.23^0	0.39	0.43	9.30%	1.10
F6	27.45^0	0.42	0.46	8.69%	1.09

Pre compression parameters of all formulations showed that they posses good flow properties.

Post compression Parameters

Table 4 Post compression parameters.

Formulation code	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Disintegration time (sec)	Drug Content %	Wetting Time (sec)	Water Absorption ratio	% Drug release
F1	3.95±0.18	4	0.75	27.62±0.05	99.7±0.04	21	95	99.1±0.09
F2	3.91±0.34	4	0.77	22.79±0.01	99.8±0.01	18	98	99.4±0.41
F3	3.70±0.18	4	0.83	40.03±0.05	99.2±0.02	29	101	94.4±0.12
F4	3.95±0.18	4	0.63	48.21±0.04	99.8±0.01	26	108	86.3±0.08
F5	3.71±0.24	4	0.88	157.12±0.04	99.6±0.01	55	112	82.7±0.14
F6	3.79±0.18	4	0.79	200.23±0.03	99.4±0.03	58	116	80.1±0.15

All values are mean ± SD, (n=3), % Drug release mean ± SD, (n=6)

All batches of tablets were evaluated for the different parameters and results are shown in table-4. Weight variation for the prepared tablets was found within specifications of USP. Hardness of the formulations F1-F6 was found within the range of 3.70±0.18-3.95±0.18kg/cm^2 which is within the acceptable limit. Friability of all formulations was within acceptable limits. The friability for all formulations was found to be less than 1% and hence the tablets with lower friability may not break during handling on machines and shipping. The drug content in different formulation was highly uniform and in the range of 99.2±0.02-99.8±0.01%.It was observed that F2 batch has least in-vitro disintegration time

and showed the wetting time in 18 seconds that was less compared to other batches. As the amount of mucilage is increased water absorption ratio also increased. Dissolution study of six formulations was performed. Formulation F2 was found to be best formulation as it releases the drug about 90.7±0.09% within one minute. Formulation F2 was also compared with Lamivir-150(Cipla), F2 was found to be best as the branded drug released only 88.3% in 10minutes compared to F2 which released about 99.4±0.41% at the end of 10 minutes.

Dissolution profile of Lamivudine Fast disintegrating tablets

Table 5: Percentage of drug release.

Time in minutes	Percentage of drug release						
	F1	F2	F3	F4	F5	F6	Lamivir-150
0	0	0	0	0	0	0	0
1	86.6±0.16	90.7±0.09	81.3±0.10	72.2±0.03	36.2±0.6	20.3±0.22	12.1
2	90.6±0.06	93.4±0.07	83.1±0.12	78.1±0.10	73.3±0.28	29.5±0.14	28.9
3	94.9±0.16	95.6±0.03	83.3±0.13	83.5±0.12	77.2±0.24	52.6±0.07	52.5
4	96.4±0.05	97.1±0.02	83.4±0.31	84.6±0.04	78.2±0.33	77.6±0.13	79.3
5	98.5±0.05	99.1±0.19	85.2±0.08	84.8±0.12	79.3±0.04	78.8±0.08	86.2
10	99.1±0.08	99.4±0.41	94.4±0.12	86.2±0.08	82.7±0.14	80.1±0.21	88.3

All values are mean ± SD, (n=6)

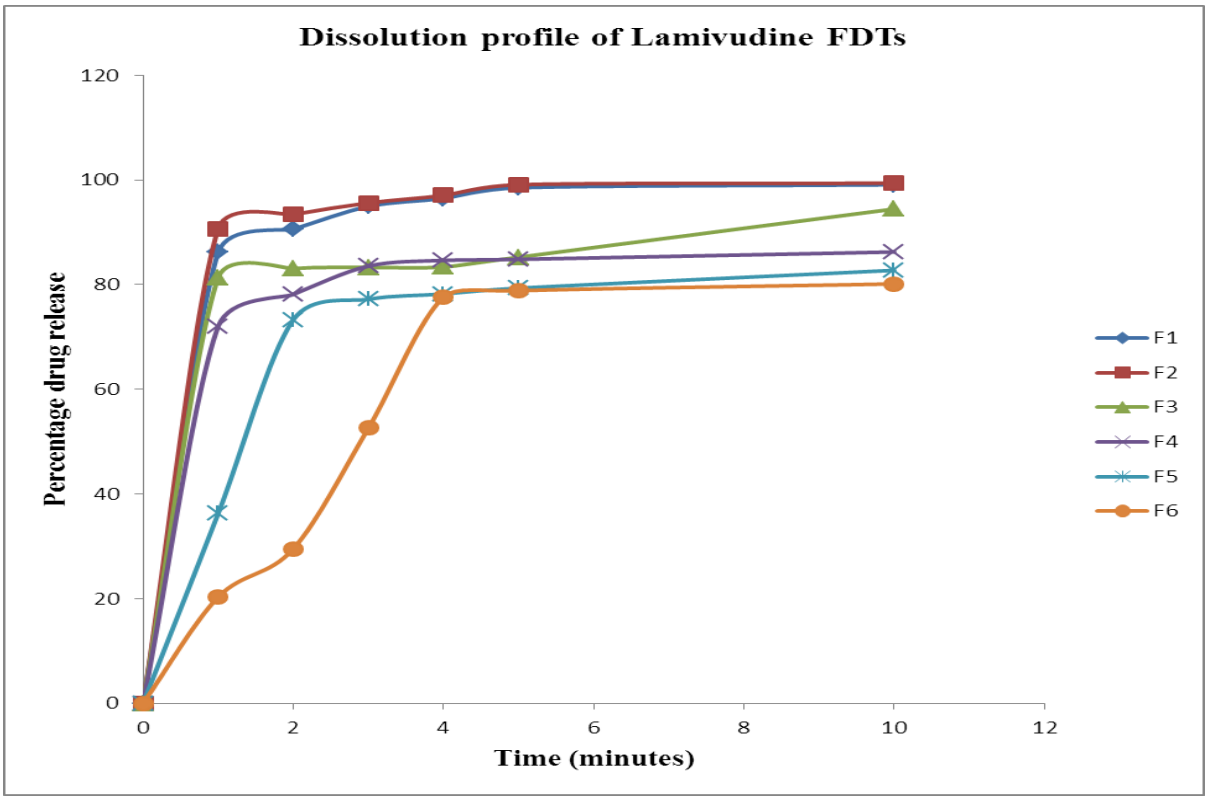


Fig 7: Dissolution profile of Lamivudine FDT.

Stability Study

Table 6: Stability study.

Evaluation test	Result
Color	White
Odor	Minty
Shape	Round with a bisect
Hardness (Kg/cm^2)	3.94±0.36
Thickness (mm)	4
Friability (%)	0.76
Disintegration time (sec)	22.08±0.01
Drug content %	99.8±0.01
Wetting time (sec)	18.3
Water absorption ratio	98
% Drug release	99.38±0.45

Stability study was conducted for F2 formulation at 40^0C and 75% RH for 30 days. Various parameters like general appearance, weight variation, hardness, friability, disintegration time, dissolution, drug content, wetting time, water absorption ratio were analyzed. There is not much variation observed in any parameters. Hence the formulation was found to be stable.

CONCLUSION

Mucilage from Ocimum basilicum was successfully extracted and characterized. Preformulation studies revealed that there is no incompatibility between drug and excipients. Six batches of Lamivudine fast disintegrating tablets using different percentages of Ocimum basilicum seed mucilage were prepared and evaluated for pre compression and post compression parameters. Among them, the formulation containing 10% mucilage has shown 22.79±0.01 seconds disintegration time. The drug content was about 99.8±0.01% and the in vitro drug release was 99.4±0.41%. In this study, it was found that on increasing the concentration of Ocimum basilicum seed mucilage above 10% there is decrease in disintegration due to the formation of viscous plug around the surface of the tablet.

ACKNOWLEDGEMENT

We are thankful to Centre for Pharmaceutical Sciences, JNTU, Hyderabad for providing the necessary facilities for carrying out this work. We are also thankful to Mylan laboratories for providing gift sample of Lamivudine.

REFERENCES

1. Karan Malik, Gurpreet Arora, Inderbir Singh, Ocimum Sanctum Seeds, a Natural Superdisintegrant: Formulation and Evaluation of Fast Melt Tablets of Nimesulide, Original papers, Polim. Med, 2012; 42(1): 49–59.

2. Mala Bhasin, *Ocimum*- Taxonomy, medicinal potentialities and economic value of essential oil, Journal of Biosphere, 2012; 1: 48-50.
3. The international pharmacopoeia, World health organization, Fourth edition, 2014.
4. Seyed M. A. Razavi, Seyed Ali Mortazavi, Lara Matia-Merino, Seyed H. Hosseini-Parvar, Ali Motamedzadegan & Elham Khanipour, Optimisation study of gum extraction from Basil seeds (Ocimum basilicum L.), International Journal of Food Science and Technology, 2009; 44: 1755–1762.
5. Sudheshnababu Sukhavasi, V. Sai kishore, Formulation and evaluation of fast dissolving tablets of amlodipine besylate by using Fenugreek seed mucilage and Ocimum basilicum gum, International Current Pharmaceutical, Journal 2012; 1(9): 243-249.
6. Patil Pradeep S, More Akshata K., Kadam Sunil, Vishwasrao Vishal, Patel Yagnik, Formulation and evaluation of orodispersible tablets of perindopril erbumine using natural superdisintegrant, Journal of Drug Delivery & Therapeutics, 2013; 3(5): 44-48.
7. Sharwaree Hardikar, Ashok Bhosale and Nilesh Jamdade, A concept proof of potential of experimental dried mucilage isolated from the seeds of ocimum basilicum as disintegrant, International Journal of Pharmacy and Pharmaceutical Sciences, 2012; 4(4): 692-695.
8. Prasad V. Kadam, Kavita N. Yadav, Sachin K. Jagdale, Rakesh S. Shivatare, Sumeet K. Bhilwade and Manohar J. Patil, Evaluation of *Ocimum sanctum* and *Ocimum basillicum* Mucilage- as a Pharmaceutical Excipient, Journal of Chemical and Pharmaceutical Research, 2012; 4(4):1950-1955.
9. Gurdeep R Chatwal and Sham K Anand, Instrumental methods of chemical analysis, X-Ray Absorption, Diffraction, and Fluorescence Spectroscopy, 2009; 2.303-2.331.
10. Sudharshan singh, Sunil B Bothara, Morphological, physico-chemical and structural characterization of mucilage isolated from the *seeds of Buchanania* lanzan Spreng, International Journal of Health & Allied Sciences, 2014; 3(1): 33-39.
11. United States Pharmacopoeia XXX NF 25 (2007). United States Pharmacopoeial Convention, Rockville.
12. C. K. Kokate, A.P. Purohit, S.B. Gokhale, Pharmacognosy, Pathway to screen Phytochemical nature of Natural drugs A.1-A.6.
13. Patil Pradeep S, More Akshata K., Kadam Sunil, Vishwasrao Vishal, Patel Yagnik, Formulation and evaluation of orodispersible tablets of perindopril erbumine using natural superdisintegrant, Journal of Drug Delivery & Therapeutics, 2013; 3(5): 44-48.

14. A. Abdul Hasan Sathali, T. Prakash, Formulation and evaluation of fast dissolving tablets of Lamivudine, International Journal of Pharmaceutical and Biological Research, 2012; 3 (3): 98-112.
15. Alay Prashanth Kumar, Formulation and evaluation of orodispersible tablets of Lamivudine, International Journal of Universal Pharmacy and Bio Sciences, 2014; 3(1): 30-44.
16. Sharma Shailesh, Hardenia Shiv Shankar and Gupta G. D., Novel In-vitro disintegration evaluation for fast dissolving tablets, Journal of Global Pharma Technology, 2009; 1(1): 113-120.
17. Stability testing of new drug substances and products Q1A (R2), ICH Harmonized Tripartite Guideline, 2003; 6-13.