Mahesh S. et al. / Vol 4 / Issue 3 / 2014 / 148-158.

International Journal of

Innovative Drug Discovery

e ISSN 2249 - 7609
Print ISSN 2249 - 7617

www.ijidd.com

DESIGN DEVELOPMENT & EVALUATION OF FAST DISSOLVING TABLET OF LACOSAMIDE

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ABSTRACT

Oral drug delivery remains the preferred route for administration of various drugs. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, and most importantly the patient compliance. Fast dissolving tablets were prepared by using different concentrations of superdisintegrants. They were prepared by direct compression and wet granulation using superdisintegrants. The Lacosamide was analyzed for spectral (IR, UV, DSC, XRD) properties. The obtained results of Lacosamide were concordant with reference specifications like IR, DSC, and XRD. The results showed that there was no interaction between the drug Lacosamide and the polymers i.e. sodium starch glycolate, Crospovidone, croscarmellose sodium, pregelatinized starch and Low-density hydroxypropyl cellulose.

KEY WORDS: Fast Dispersable Tablet. Lacosamide. *In Vitro* dispersion.

INTRODUCTION

Recent advancements in novel drug delivery systems have resulted in a convenient dosage form for administration and to achieve better patient compliance known as fast dissolving tablets (FDTs). FDT is "Solid unit dosage form containing a medicinal substance that disintegrates rapidly and dissolves in the mouth as soon as they come in contact with saliva without the need of water or chewing [1-3]. The faster the drug into solution form, quicker the absorption and onset of actions. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. A fraction of pregastric drug absorption may bypass the digestive system and metabolism by the stomach acids and enzymes. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form. The mouth dissolving solid dosage form turns into a soft paste or liquid form on administration. This kind of property in dosage form can be added by inclusion of right disintegrants which play key role in formulation of mouth dissolving tablets. Addition of disintegrants in fast dissolving tablets, leads to quick disintegration of tablets and hence improve dissolution. As disintegration plays an important role in a tablet's dissolution before the active drug substance is finally released from the tablet's structure into the body therefore type, concentration, and efficiency of disintegrants to a large extent affects the disintegrant properties (e.g., disintegration time [DT] and the ratio of crushing strength–friability to disintegration time [CSFR/DT]) of formulated tablet [4-6].

They are known by various names such as "fast-melting, fast-dissolving, oral disintegrating or orodisperse or Mouth dissolving". The European Pharmacopoeia defines the term "orodisperse" as a tablet that can be placed in the mouth where it disperses rapidly before Swallowing. The US Food and Drug Administration Center for Drug Evaluation and Research (CDER) defines, in the 'Orange Book', an ODT as "a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue.The significance of these dosage forms is highlighted by the adoption of the term, "Orodispersible Tablet", by the European Pharmacopoeia which describes it as a tablet that can be placed in oral cavity where it disperses rapidly before swallowing. United States Food and Drug Administration (USFDA) had also approved these dosage forms as term "Orodispersible tablet" and defined as "A solid dosage form containing medicinal substances or an

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active ingredient along with super disintegrants, which help them to dissolve the tablets within a minute. The growing importance of fast dissolving was underlined recently when European pharmacopoeia adopted the term "Orodispersible tablet" as a tablet that to be placed in the mouth where it disperses rapidly before swallowing. According to European pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes [7-10].

MATERIALS AND METHODS

Formulation of Fast Dissolving Tablet

In the present work, direct compression method and wet granulation method was adopted with the aid of superdisintegrants for the preparation of rapid dissolving tablets of Lacosamide. Lacosamide tablets are available in 50mg, 100mg, 150mg, 200mg, and 250mg doses in the market. Dose of 50mg is selected for present study. Development of the formulation in the present was mainly based on the type, method of addition and concentration of polymers[11,12].

By addition of super Disintegrants

Lacosamide fast dissolving tablets were manufactured by direct compression in formulations F1 to F5 using superdisintegrants [Ac-Di-Sol (10%), Sodium starch glycolate (12.5%) Crospovidone (6%) Pregelatinised starch (15%), L-HPC (7%)]. The ingredients depicted in Table.1 (except magnesium stearate and talc) were passed through sieve # 60, mixed homogenously and co grind in a mortar and pestle[13-17]. Finally Talc and magnesium stearate were passed through sieve # 60, mixed and blended with initial mixture. Then it is mixed for 5min. The mixed blend of drug and excipients was compressed into tablet to produce convex faced tablets of 200mg using 8 mm round punches on multipunch tablet compression machine. A batch of 50 tablets was prepared for each of the designed formulations (Table 1).

Wet granulation

Lacosamide fast dissolving tablets were manufactured by wet granulation in five formulations (W1 to W5) using superdisintegrants [Ac-Di-Sol (17%), Sodium starch glycolate (20%) Crospovidone (10%), Pregelatinised starch (20%), L-HPC). In this partly intrangular and extrangular technique was adopted. All the ingredients were passed through sieve # 60 mesh separately [17-20]. Then the granules were prepared with intragranularingredients using starch paste as a binder passing lumps through sieve # 44 mesh. Then extragranular ingredients in table were weighed and mixed in geometrical order withprepared granules and compressed (Table 2, 3).

Evaluation of Lacosamide tablets

Drug-polymer compatibility studies

In the preparation of tablets formulations, drug and polymer may interact as they are close contact with each other, which could be lead to instability of the drug. Preformulation studies regarding the drug-polymer interaction are therefore very critical in selecting appropriate polymers. FTIR spectroscopy was employed to ascertain the compatibility between Lacosamide and the selected polymers. Potassium bromide, pure drug and polymers were kept in hot air oven to remove moisture content if present [15,16]. The FTIR analysis of the sample was also carried out for qualitative compound identification. The pellet of approximately 01 mm diameter of the drug and formulation were prepared in pressure compression machine. The sample pellet was mounted in FTIR compartment and scanned at wavelength 4000 cm^{-1} – 500 cm^{-1}. The spectrum obtained for drug-polymer was compared with pure Lacosamide spectra.

Determination of drug content

Tablets were selected randomly and average weight was calculated. Tablets were crushed in a motor and accurately weighed amount of tablet powder was taken from the crushed blend. Then the samples were transferred to 100ml volumetric flask and diluted with phosphate buffer (pH 6.8) solution. The contents were shaken periodically and kept for 2hrs for solvation of drug completely. The mixture was filtered in Whitmann filter paper and absorbance was measured at 257nm using phosphate buffer as a blank. The drug content in each tablet was calculated using standard calibration curve of Lacosamide.

In vitro Drug Release

- **Calibration of Lacosamide in phosphate buffer (pH6.8) solution at λ_{max} 257nm**

The procedure for calibration curve of Lacosamide is same as mentioned under drug content determination section.

- **Preparation of standard stock solutions**

Accurately weighed 10 mg of Lacosamide was transferred into 100 ml volumetric flask and dilute up to the mark with distilled water to get stock solutions containing 100µg/ml Lacosamide.

- **Procedure for determination of In vitro drug release**

In vitro rug release of the tablets was carried out using USP – type II dissolution apparatus (paddle type). The dissolution media, 900ml of phosphate buffer (pH6.8) solution, was placed into dissolution flask maintaining the temperature of 37±0.5º and rpm of 50. One tablet was placed in each flask of dissolution apparatus. The apparatus was allowed to run. Samples measuring 5ml were withdrawn after every 2min interval of 0, 2,4,6,8. Samples were filtered through 10µm Whatmann filter paper. The fresh dissolution medium was replaced every time to maintain sink conditions. The collected samples were analyzed at 257nm using media as blank. The cumulative drug release was calculated. The released data obtained was

fitted into Higuchi mathematical model.

X-Ray Diffraction

In drug design, discovery, development and formulation process, X-ray powder diffraction can help to establish a formulation by knowing the morphology and the degree of crystallinity, to provide unique polymorph identification and determine the quantity of each in mixture. With XRD, non-ambient analysis can also be performed to study moisture influence on physical properties of drugs.

Differential Scanning Calorimetry (DSC)

Differential scanning Calorimetry (DSC) used to measure the heat loss or gain resulting from physical or chemical changes within a sample as a function of temperature. Crystallization and degradation are usually exothermic processes. Quantitative measurements of these processes have many applications in preformulation studies including purity, polymorphism, salvation, degradation, and excipients compatibility.

Accelerated stability study

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.

In order to determine the change in *In-vitro* release profile on storage, stability study of batch W4 was carried out at 40°C ± 2°C/75% RH ± 5% RH and25°C ± 2°C/60% RH ± 5% RH. Sample were withdrawn at various intervals the study was conducted for 90 days interval and evaluated for change in *Invitro* drug release pattern, hardness, wetting time, percent drug content and disintegration time

Calibration curve data

The calibration curve of Lacosamide was prepared in Phosphate buffer (pH 6.8). The slope and correlation coefficient values were found to be 0.0009 and 0.999 respectively.

Infrared Spectral Assignment

The pellet of approximately 01 mm diameter of the drug was prepared grinding 3-5 mg of sample with 100-150 mg of Potassium Bromide using hydrostatic press. The sample pellet was mounted in IR compartment and scanned at wavelength 4000 cm^{-1} – 500 cm^{-1}. The results were shown in figure 1.

Differential Scanning Calorimetry (DSC)

DSC analysis was performed on 5 mg sample. Samples were heated in an open aluminum pans at a rate of 10^0 per min in a 0 to 200^0C temperature range under a nitrogen flow of 40 mL/min. It shows endothermic peak at about 145.35^0Cshown in Figure 2.

X ray Diffraction Study

The powder X-ray diffraction analysis shows that, the prominent peaks of pure drug Lacosamide at 2θ 3, 12, 16, 17, 18, 20, 21, 26, 32, 37, and 42 are due to the presence of drug in crystalline nature. The results are given in figure 3.

Ultraviolet Absorption Maxima:

Ultraviolet absorption in the range 200 to 400 nm of a 500µg/ml solution of Lacosamide in phosphate buffer (pH 6.8) was scanned. The absorption maximum (λmax) of Lacosamide was found to be 257 nm which is shown in figure 4.

Characterization of Lacosamide Tablets

Post compression parameters

The Lacosamide tablets were prepared by direct compression and wet granulation methods. The tablets were evaluated for weight variation, hardness, friability, disintegration time, water absorption ratio, wetting time, drug content dissolution, and test for dispersion. The results of physicochemical evaluation of prepared tablets are shown in table 5.

- The hardness was in the range of 1.0 to 4.0 kg/cm^2 and in all the cases the friability was less than 1%.
- The drug content of all the formulations was found to be in the range of 98.87% to 101.12.
- The disintegration time of all the formulations was found to be 14
- The wetting time (completely wetting tablet – figure 7-9) of all the formulated tablets was in the range of 22 to 64 Sec.
- The water absorption ratio was found to be in the range of 60.19% to 100.06% and in all the cases the tablet passes the test for dispersion.

Study Storage condition Minimum time period covered by

Long term* 25°C ± 2°C/60% RH ± 5% RH **or** 30°C ± 2°C/65% RH ± 5% RH 3 to 6 months

Intermediate** 30°C ± 2°C/65% RH ± 5% RH 3 to 6 months

Accelerated** 40°C ± 2°C/75% RH ± 5% RH 3 to 6 months

Accelerated stability studies

Fast dissolving tablets W4 were kept for accelerated stability studies at 40°C ± 2°C/75% RH ± 5% RH and 25°C ± 2°C/60% RH ± 5% RH for 3 months using desiccators and hot air oven.

Active substances intended for storage in a refrigerator

Long term 5° C ±3° C 6 months (option a and b)

Accelerated 25° C ±2° C/60% RH ±5% RH 3 to 6 months.

RESULTS AND DISCUSSION

Table 1. Formulation of FDT using direct compression method

Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)
Lacosamide	50	50	50	50	50
L-HPC	-	-	-	14	-
Sodium Starch Glycolate	-	-	-	-	25
Pregelatinised starch	-	-	30	-	-
Crospovidone	12	-	-	-	-
Croscarmellose sodium	-	20	-	-	-
MCC	40	40	40	40	40
Pearlitol SD200	93	85	75	91	80
Sodium saccharin	1	1	1	1	1
Magnesium stearate	1	1	1	1	1
Talc	2	2	2	2	2
Flavour	1	1	1	1	1
Total wt per tablet (mg)	200	200	200	200	200

L-HPC – Low substituted hydroxy propyl cellulose; MCC –Microcrystalline cellulose

Table 2. Formulation of FDT using wet granulation method (Intragranular)

Intragranular	W1(mg)	W2(mg)	W3(mg)	W4(mg)	W5(mg)
Lacosamide	50	50	50	50	50
Sodium Starch Glycolate	-	-	25	-	-
Crospovidone	-	-	-	15	-
Pregelatinised starch	-	-	-	-	25
L-HPC	18	-	-	-	-
Croscarmellose sodium	-	25	-	-	-
MCC	30	30	30	30	30
Pearlitol SD200	37	30	25	45	25
Sodium saccharin	1	1	1	1	1

Table 3. Formulation of FDT using wet granulation method (Extra granular

Ingredients	W1 (mg)	W2 (mg)	W3 (mg)	W4 (mg)	W5 (mg)
Extragranular					
Sodium Starch Glycolate	-	-	15	-	-
Crospovidone	-	-	-	5	-
Pregelatinised starch	-	-	-	-	15
L-HPC	10		-	-	-
Croscarmellose sodium	-	10	-	-	-
Talc	2	2	2	2	2
Magnesium stearate	1	1	1	1	1
Flavour	1	1	1	1	1
Total weight per tablet	150	150	150	150	150

L-HPC – Low substituted hydroxyl propyl cellulose

Table 4. Interpretation of pure Lacosamide

Functional group	Range	Peak
Aromatic ring	3100 – 3000 cm^{-1}	3290, 3027 cm^{-1}
Carbonyl group	1760 – 1600 cm^{-1}	1636 cm^{-1}
Amine	3400 – 3500 cm^{-1}	3290 cm^{-1}
Ether	1260 – 1000 cm^{-1}	1137 cm^{-1}

Table 5. Characterization of Lacosamide fast dissolving tablets

Parameters / Formulations	Thickness* (mm)	Weight variation (%)	Friability (%)	Hardness* (kg/cm^2)
W1	4.2±0.5	1.35	0.315	3.0±1.5
W2	4.2±0.8	1.65	0.321	4.0±1.0
W3	4.3±0.6	1.03	0.336	3.5±0.5
W4	4.2±0.8	1.54	0.367	4.0±0.5
W5	4.3±0.6	1.76	0.345	2.0±2.0
F1	4.9±1.0	1.43	0.540	2.0±1.5
F2	4.8±0.8	1.14	0.539	1.0±2.0
F3	4.9±0.5	1.89	0.628	1.5±2.0
F4	4.9±0.4	1.97	0.589	1.0±1.5
F5	4.9±0.8	1.38	0.608	2.0±1.5

* Data are expressed as mean ± S.D. (n = 3)

Table 6. Characterization of Lacosamide fast dissolving tablets

Parameters / Formulations	Wetting time* (sec)	Water absorption ratio (%)	Test for dispersion*	In-vitro disintegration time (sec)*
W1	42±0.5	91.21	Passes	35±0.7
W2	38±1.0	78.26	Passes	25±1.0
W3	47±.40	82.97	Passes	37±0.5
W4	22±1.0	100.06	Passes	14±1.0
W5	34±0.6	60.19	Passes	28±0.8
F1	51±1.0	74.73	Passes	32±1.0
F2	55±2.0	82.13	Passes	36±0,5
F3	50±1.5	72.82	Passes	33±1.0
F4	53±2.0	96.84	Passes	32±1.5
F5	64±0.5	78.28	Passes	48±0.5

*Data are expressed as mean ± S.D. (n = 3)

Table 7. Characterization of Lacosamide fast dissolving tablets (Drug content)

Formulations	Drug content	
	(%)	(mg)
W1	100.71	50.355
W2	98.87	49.435
W3	99.42	49.71
W4	100.14	50.07
W5	99.84	49.92
F1	99.12	49.56
F2	99.74	49.87
F3	101.12	50.56
F4	98.96	49.48
F5	99.28	49.64

Data of *in vitro* drug release studies

Table 8. *In vitro* drug profile of Lacosamide for formulations by wet granulation method (W1 – W5)

Time/Min	W1	W2	W3	W4	W5
0	0	0	0	0	0
2	19.56±0.5	15.48±0.8	20.44±1.0	42.37±1.5	16.73±2.0
4	48.26±2.0	42.59±1.0	42.16±2.0	82.18±2.5	36.05±3.0
6	63.91±1.0	73.56±2.0	69.0±3.0	99.34±2.0	65.66±2.5
8	99.13±2.5	95.5±1.5	88.16±1.5	99.34±3.0	87.55±3.5
10	99.13±3.0	95.5±2.0	100.94±2.0	99.34±3.0	98.42±3.0

Data are expressed as mean ± S.D. (n = 3)

Table 9. In *vitro drug* release profile of Lacosamide tablet for formulations by direct compression method (F1 – F5)

Time/Min	F1	F2	F3	F4	F5
0	0	0	0	0	0
2	36.1±1.5	30.99±1.5	14.22±1.0	36.1±2.0	18.13±2.0
4	52.86±3.0	60.68±0,50	34.91±2.0	58.27±1.0	37.56±3.0
6	96.78±2.0	82.64±2.5	53.02±3.0	77.36±3.0	58.27±2.5
8	100.54±0.50	100.71±1.0	85.35±2.0	100.87±2.0	75.11±1.5
10	100.54±1	100.71±2.0	101.45±1.0	100.87±1.0	98.42±3.0

Data are expressed as mean ± S.D. (n = 3)

Table 10. Higuchi model release profile for Lacosamide tablets for formulations F1 to F5

Square root of Time	F1	F2	F3	F4	F5
1.414	36.1	30.99	14.22	36.1	18.13
2	52.86	60.68	34.91	58.27	37.56
2.449	96.78	82.64	53.02	77.36	58.27
2.828	96.78	100.71	85.35	100.87	75.11
3.162	96.78	100.71	101.45	100.87	98.42

Table 11. Higuchi Model Release Profile for Lacosamide tablets for formulations W1 to W5

Square root of Time	W1	W2	W3	W4	W5
1.414	19.56	15.48	20.44	42.37	16.73
2	48.26	42.59	42.16	82.18	36.05
2.449	63.91	73.56	69	99.34	65.66
2.828	99.13	95.5	88.16	99.34	87.55
3.162	99.13	95.5	100.94	99.34	98.42

Table 12. Stability data of Lacosamide tablets (Formulation - W4)

Parameters	Days	40°C ± 2°C/ 75% RH ± 5%	25°C ± 2°C/ 60% RH ± 5%
Hardness	0	4.0	4.0
	30	4.1	4.0
	60	4.0	3.5
	90	3.8	3.7
Wetting time	0	22	22
	30	22	21
	60	20	22
	90	20	24
Disintegration time	0	14	14
	30	14	15
	60	12	14
	90	16	15
Drug content (mg)	0	50.07	50.07
	30	49.86	49.83
	60	49.29	49.37
	90	49.02	48.67

Table 13. In-vitro drug release profile of Lacosamide for formulation W4 after stability

Time	% Drug release at 40° C	% Drug release at 25° C
0	0	0
2	42.59	37.56
4	77.46	75.35
6	98.93	98.23

Data are expressed as mean ± S.D. (n = 3)

Table 14. Drug degradation for formulations W4 after stability

Days	Drug content at 40°C (mg)	Drug content at 25° C (mg)
0	50.07	50.07
30	49.86	49.83
60	49.29	49.37
90	49.02	48.67

Fig. 1. IR Spectra of Lacosamide

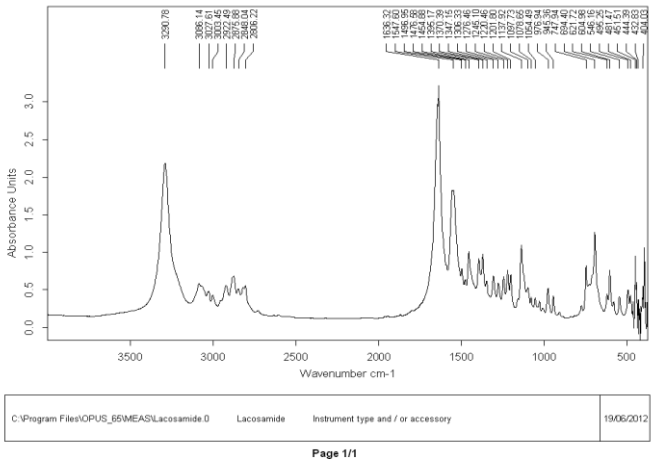


Fig. 2. DSC of Lacosamide

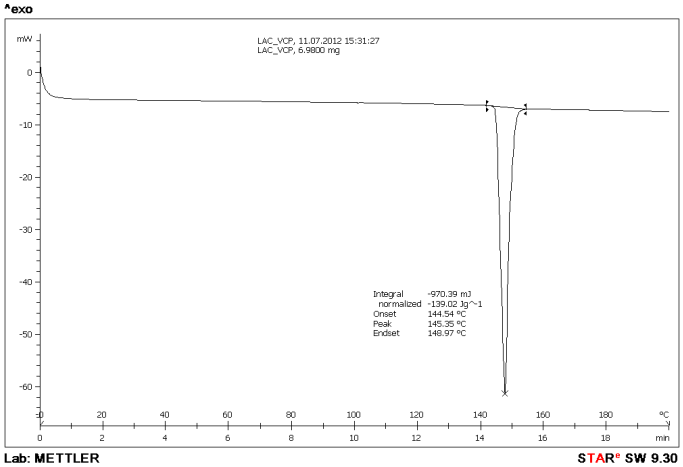


Fig. 3. XRD of Lacosamide

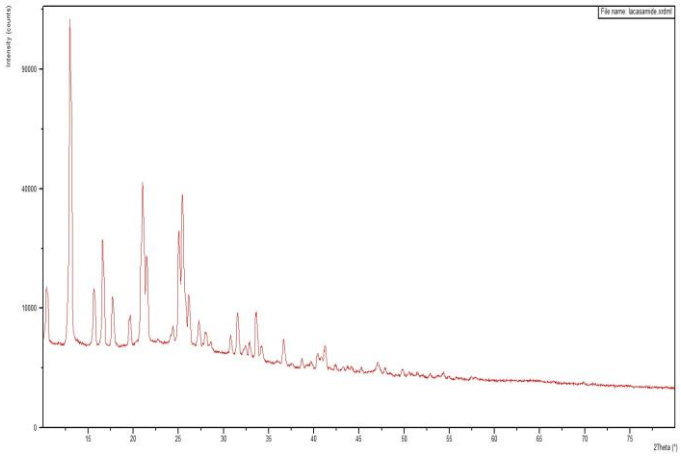


Fig. 4. Scan of Lacosamide

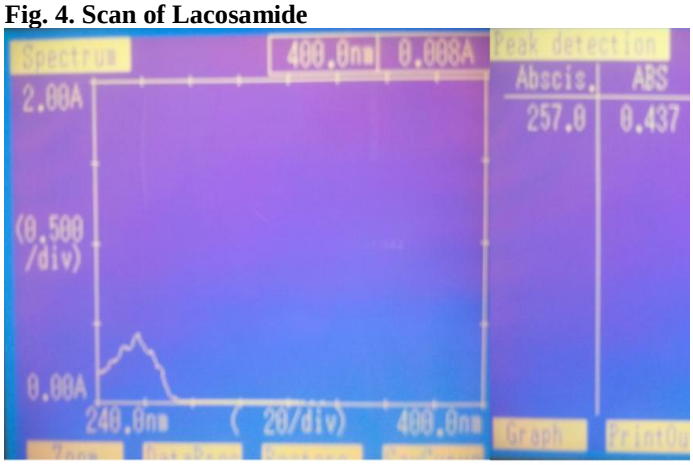


Fig. 5. IR Spectra of formulation W4

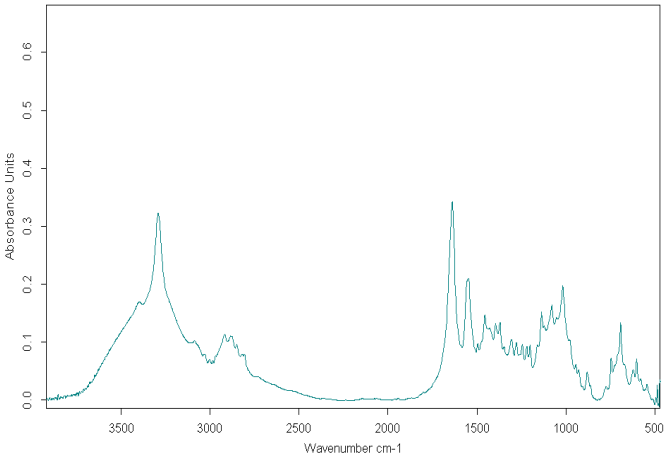


Fig. 6. IR Spectra of formulation F1

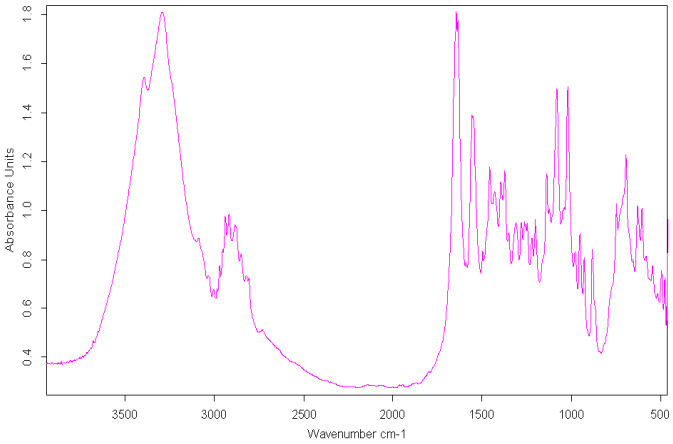


Fig. 7. DSC of formulation (W4)

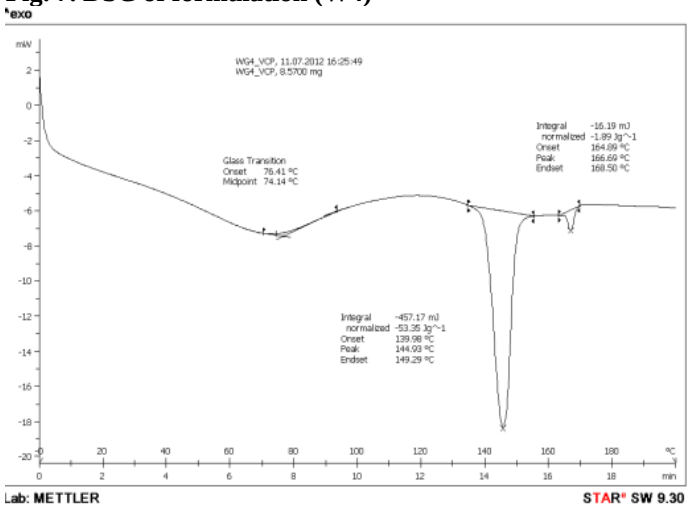


Fig. 8. XRD of formulation (w4)

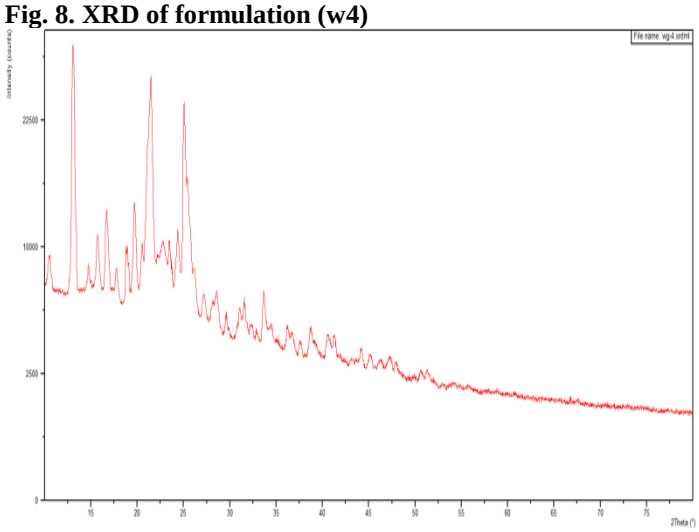


Fig. 9. XRD of formulation (F1)

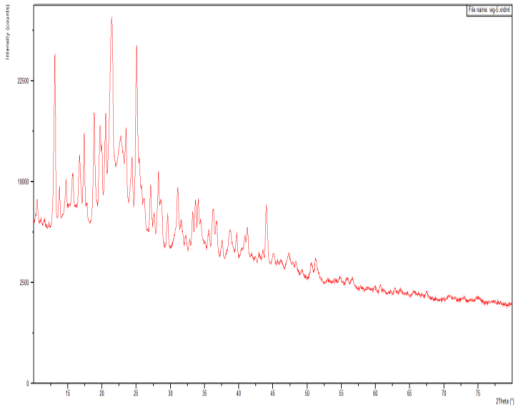


Fig. 10. Lacosamide tablets

Fig. 11. Completely wetted tablet (W4)

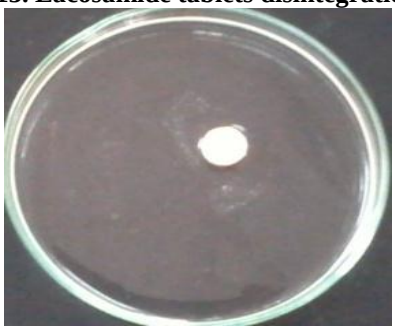
Fig. 12. Lacosamide tablets disintegration formulation F1

0 seconds

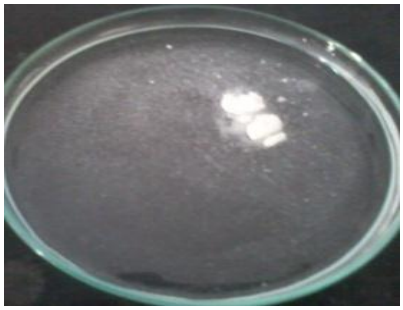
20 seconds

40 seconds

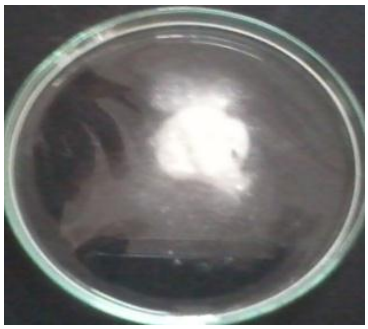
Fig. 13. Lacosamide tablets disintegration formulation W4



0 seconds



10 seconds



20 seconds

Fig. 14. *In vitro* drug profile of Lacosamide for formulations by wet granulation (W1 – W5)

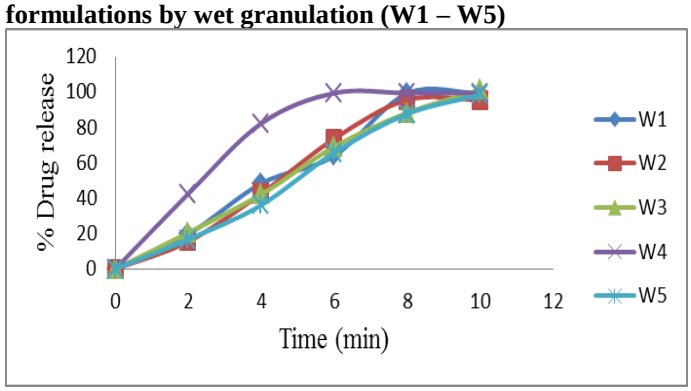


Fig 15. *In vitro* drug profile of Lacosamide tablets for formulations (F1 – F5)

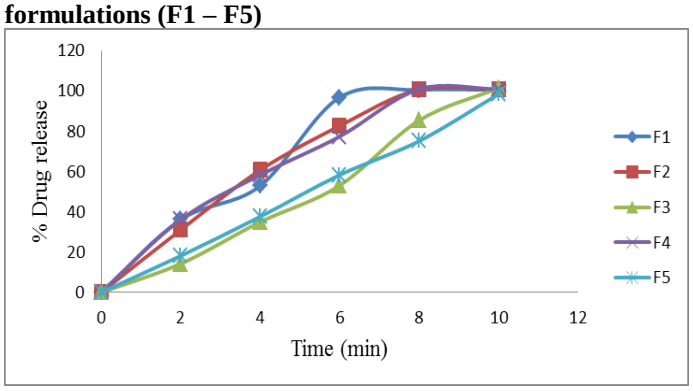


Fig 16. Higuchi model release profile for Lacosamide tablets for formulations F1 to F5

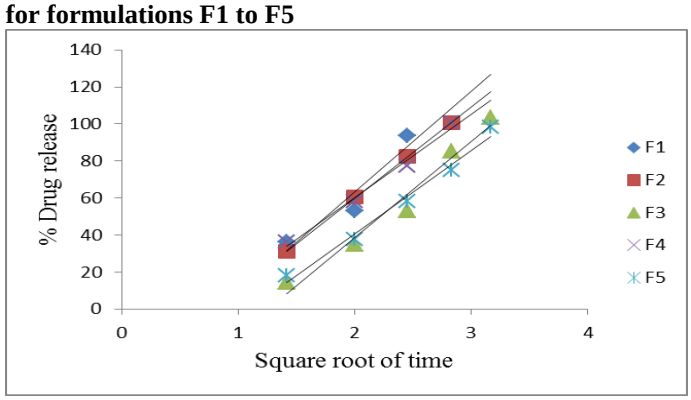


Fig. 17. Higuchi Model Release Profile for Lacosamide tablets for formulations W1 to W5

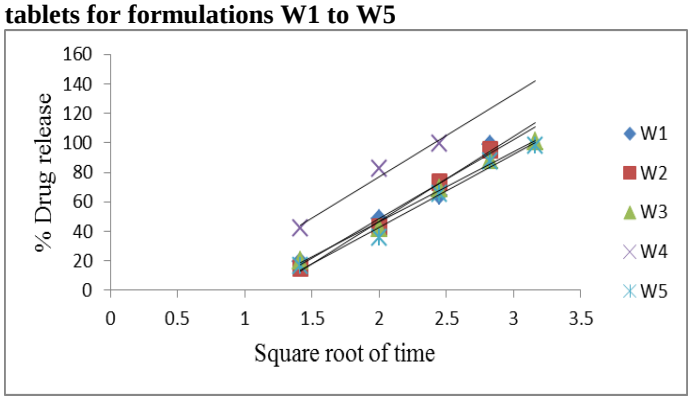
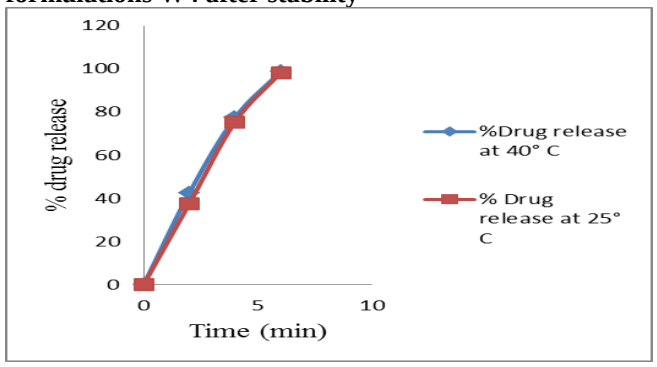


Fig. 18. In vitro drug release profile of Lacosamide for formulations W4 after stability



FT-Infrared spectroscopy to find out the compatibility of drug with polymer

This study was carried out to find out the possible interaction between the selected drug Lacosamide and the polymers Crospovidone, sodium starch glycolate, croscarmellose sodium, L-HPC, pregelatinized starch. FT-IR of lacosamide show the following characteristics peaks Aromatic ring-3290, 3027 cm^{-1}, Carbonyl group-1636 cm^{-1}, Amine-3290 cm^{-1}, Ether-1137 cm^{-1} (Figure 1,5,6).

DSC study to find out the compatibility of drug with polymer

This study was carried out to find out the possible interaction between the selected drug Lacosamide and the polymer (Crospovidone). DSC of Lacosamide showed a sharp endothermic peak at 145.35°C corresponding to its melting point. The DSC analysis of Formulation (W4) revealed negligible change in the melting point of Lacosamide (144.93°C). The retention of this characteristic endothermic peak of the drug (Figures 2,7), thus revealing compatability of the selected drug with polymer.

XRD study to find out the compatibility of drug polymer

This study was carried out to find out the interaction between selected drug Lacosamide and polymer. In this study Lacosamide exhibited characteristics diffraction pattern which was compared with pure drug XRD which was shown in figures 8,9.

Preparation of Lacosamide tablets

The Lacosamide tablets were prepared by direct compression method and wet granulation methods. Sodium starch glycolate, Crospovidone, croscarmellose sodium, L.HPC, pregelatinized starch as super disintegrants and microcrystalline and mannitol as a diluent. Sodium saccharin is used as a sweetening agent. The orders of disintegration time among super disintegrates are Crospovidone> L.HPC > croscarmellose sodium > sodium starch glycolate > pregelatinized starch. This finding is in agreement with results obtained from wetting time, since

Crospovidone swells with more gelling than other superdisintegrants, which extend disintegration time as a result. It is observed that the disintegration time of tablets decreased with increasing concentration of superdisintegrants. In case of Lacosamide and Crospovidone formulation which act by capillary action which might have formed a thick barrier to further penetration of the disintegration medium and hindered the disintegration of tablet contents.

Characterization of Lacosamide tablets

Pre compression parameters

The prepared Lacosamide tablets blends were evaluated for angle of repose, bulk density, tapped density and compressibility index. The bulk densities of the tablet blends were found to be in the range of 0.451 to 0.668 gm/ml and the tapped density ranged from 0.522 to 0.754 gm/ml. The flow characteristics of the tablets blend were assessed by determined their angle of repose. The values of compressibility indexes were in the range of (11.36 to 14.36%) and angle of repose varied from (24.26º to 31.02º) signifies reasonably good flow properties of the tablet blends for all the formulations thus ensuring homogenous filling of dies. The Hausner's ratio of all formulation blends was found to be less than 1.2 indicates better flow properties.

Post compression parameters

The Lacosamide tablets were prepared by direct compression and wet granulation methods and the results are shown in the tables. The tablets were evaluated for its weight variation, drug content, hardness, friability, wetting time, water absorption time, and test for dispersion. Tablet hardness test is measure of the cohesiveness of tablets and it plays a vital role for drug release. It is one of the official methods for the determination of tablet strength. The other essential requirements of tablets are to have an acceptable friability to withstand shocks during packing and shifting. Hardness must be controlled to ensure that the product is firm enough to withstand handling without breaking or crumbling and not so hard that the disintegration time is unduly prolonged. The thickness of the tablet was found to be 4.2 – 4.9mm. The weight variation of the prepared tablet was found to be 1.03 – 1.97%. So it was predicted that all the tablets exhibited uniform weight with low standard deviation values within the acceptable variation as per IP. The results are shown in Table 5. The friability of all the formulations was found to be less than 1.0 %, which indicates the tablet's ability to withstand abrasion in handling, packaging and shipment. The hardness of tablet was varied from 1.0 – 4.0 kg/cm^2, which have satisfactory strength to withstand with the applied mechanical shocks. A disintegrant was incorporated in all the formulations to facilitate a breakup or disintegration of the tablet when it contacts with water or saliva in mouth. Disintegrants drawing the water into the tablet causes swelling and burst apart. The disintegration time of all the formulations was found to be in between 14.0 – 48.0 sec. The results are shown in Table 6. The *in-vitro* wetting time of all the formulations was varied in between 22.0 – 64.0 sec. The results were shown in Table 6. The drug content of all the tablet formulations was determined spectrophotometrically at 257 nm. It varied from 49.48 – 50.56mg per tablet. The correlation of variation was found to be less than 0.5, indicating uniformity of the drug content in the prepared tablets. The results of the content uniformity and percent drug content were shown in Table 7.

***In vitro* drug release studies**

Dissolution testing has become a mandatory requirement for several oral dosage forms. Dissolution testing is an integral component in pharmaceutical research and development of solid dosage forms. *In-vitro* release of Lacosamide from the prepared fast dissolving tablets was studied in phosphate buffer pH 6.8 for 12 minutes. The results of dissolution profile are shown in Table 8, 9 and Figure 14, 15. Formulations W4 and F1 which contains Crospovidone release was found to be 99.34 and 95.78 respectively. The formulation with Crospovidone shows more release than the tablets with other super disintegrants. Next the release data obtained were subjected for the kinetic treatment to know the type and order of drug release.

The obtained data from *in-vitro* Drug release was fitted in Higuchi model, represents graphically as Cumulative percentage drug release v/s Square root time. The R^2 value for W1 to F5 found to be 0.9636, 0.9931, 0.9933, 0.977, 0.9847, 0.9447, 0.9872, 0.9908, 0.9986 and 0.9982 respectively.

Stability studies

The stability study was performed for W4 formulation according to ICH guidelines at 40°C ± 2°C/75% RH ± 5% RH and25°C ± 2°C/60% RH ± 5% RH showed that the formulation was stable after three months as there is no significant change in the hardness, disintegration time, wetting time and drug content (Table 12). Dissolution profile of W4 formulation after stability period of three months did not show any variation in drug release which indicates formulation was stable.

CONCLUSION

The objective of the present study was to formulate and evaluate fast dissolving drug delivery system for an anti-epileptic drug. In this study, fast dissolving tablets were formulated with adequate mechanical strength using different superdisintegrants and evaluated for various *in-vitro* parameters.

Fast dissolving tablets were prepared by using different concentrations of superdisintegrants. They were prepared by direct compression and wet granulation using superdisintegrants (Ac-Di-Sol, Sodium starch glycolate, Pregelatinised starch, Low-density hydroxypropyl cellulose

and Crospovidone). The tablets were evaluated for their organoleptic (Colour, Odour), physical (Size, Shape and Texture) and quality control parameters (Thickness, Hardness, Friability, Disintegration Time and Wetting Time).

The Lacosamide was analyzed for spectral (IR, UV, DSC, XRD) properties. The obtained results of Lacosamide were concordant with reference specifications like IR, DSC, and XRD. The results showed that there was no interaction between the drug Lacosamide and the polymers i.e. sodium starch glycolate, Crospovidone, croscarmellose sodium, pregelatinized starch and Low-density hydroxypropyl cellulose.

The disintegration properties of tablet were observed as Crospovidone > Low-density hydroxypropyl cellulose > Croscarmellose sodium > Sodium starch glycolate > Pregelatinised starch. The rapid drug dissolution might be due to the easy and fast breakdown of tablet and rapid absorption of drug into the dissolution media.

The drug release was found as W4 < F1 < F4 < F2 < W1 < W2< F3 < W3 < W5 < F5.The selected tablets formulations which posses the best physical quality were W4 and F1 which were prepared by wet granulation and direct compression methods respectively.. On experimental data it was concluded thatfast dissolving tablet of Lacosamide would be an effective alternative approach for management of seizures. Superdisintegrants Crospovidone in formulation (W4 and F1) formulation is the most promising dosage form for rapid release of Lacosamide tablets. It also found to be that there is no interaction between the drug and polymer (Crospovidone) in formulations W4 and F1. Further it can be concluded that on comparing best formulations (F1 Direct compression and W4 Wet granulation) weight of wet granulation (W4) is less compared to that of direct compression which is one of the main criteria of fast dissolving tablet and wet granulation method produce more harder tablets than direct compression which proves that wet granulation is most suitable method in formulation of fast dissolving tablets of Lacosamide.

AKNOWLEDGEMENTS

The authors are grateful to Medreich Limited, Bangalore, for providing gift sample of the drug. The authors are also grateful to the chairman and the principal of Krishna Teja Pharmacy College, Tirupati for providing facilities to carry out the research work.

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