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Formulation and Evaluation of Fast Dissolving tablet of Anti-hypertensive Drug

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ABSTRACT: For treatment or management of diseases, oral delivery is giving much more attention from the ancient decade. A new concept in oral delivery is mouth dissolving tablets (MDTs) are widely accepted nowadays. Mouth dissolving tablets are solid dosage forms which, when placed in the mouth, disintegrate, dissolve and release active agent within a few minutes without the need for water. It has more significance to geriatric, Pediatric, bedridden patients because they have a problem in swallowing and the patient with dysphasia. It is more useful for the traveler and busy patients who don't have easy access to water. Mouth dissolving tablets are prepared by various technologies with the aid of superdisintegrants. Mouth dissolving tablets are more reliable than conventional dosage forms like tablets, capsules because of better patient compliance. The advancement in this field allows the development of an economic and better way of disease management with avoidance of several problems related to the other delivery systems.

Keywords: Mouth dissolving tablets, Superdisintegrants, Evaluation

I. INTRODUCTION:

Orally disintegrating tablets (ODT) this dosage form is chosen when the patient has difficulty in swallowing (Lindgren et al., 1993), and it's also suitable for use in geriatric and pediatric patients, or for those who suffering from various conditions such as dysphagia (Sastry et al., 2000).

Orally disintegrating tablets are also called orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapidly melts (Fu et al., 2004; Fernandes et al., 2009). However, of all the above terms, the United States Pharmacopoeia (USP) approved these dosage forms as orally disintegrating tablets or ODTs (Guidance for Industry: Orally Disintegrating Tablets, 2008). Recently, the European Pharmacopoeia 7th edition has used the term orodispersible tablet for tablets that disperse inside the mouth cavity and within few second before swallowing (European Pharmacopoeia, 2011a). The United States Food and Drug Administration (FDA) defined ODT as 'a solid dosage form containing a medicinal substance or active ingredient which disintegrates rapidly usually within a few seconds when placed upon the tongue' (Guidance for Industry: Orally Disintegrating Tablets, 2008).

Materials and Methods:

Material	Specification/Grade	Manufacturer/Supplier.
Enalapril	Research grade	Amsal Chem Pvt. Ltd. Mumbai.
Guar gum	Research grade	Fine Chemie Pvt. Ltd. Pune.
Sodium starch glycolate	Research grade	Fine Chemie Pvt. Ltd. Pune.
Microcrystalline cellulose	Research grade	Fine Chemie Pvt. Ltd. Mumbai.
Mannitol	Research grade	Loba Chemie Pvt. Ltd. Mumbai.

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Magnesium stearate	Research grade	Loba Chemie Pvt. Ltd. Mumbai.
Talc	Research grade	Loba Chemie Pvt. Ltd. Mumbai.
NaOH	Analytical reagent	Loba Chemie Pvt. Ltd. Mumbai.
KH_2PO_4	Analytical reagent	Loba Chemie. Pvt. Ltd. Mumbai.

Formulation of fast dissolving tablets of Enalapril :

FDTs were prepared by D.C. By using drug + polymer + excipients

↓

Required qty of E + GG + SSG + MCC + Mannitol + mg. Stearate + Talc

↓ Seive no 60

Drug + above excipients for 10 min to achieve homogeneous blend

↓

Add mg stearate with above homogeneous blend for 3 min.

↓

Finally powder was compressed into tablets by tablet punching machine

↓

Thus formulations (F1 to F6) were prepared using optimized conc. of polymer like SSG -2 to 6 mg, GG 2 to 6 mg, MCC 100 mg, mannitol 80 to 84 mg , mg stearate 2 mg and Talc 2 mg

Formulation of fast dissolving tablets of Enalapril.

Composition of fast dissolving tablets of Enalapril.

Ingredient(mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Enalapril	10	10	10	10	10	10
Sodium starch glycolate	-	-	-	2	4	6
Guar gum	2	4	6	-	-	-
Microcrystalline cellulose	100	100	100	100	100	100
Mannitol	84	82	80	84	82	80
Magnesium stearate	2	2	2	2	2	2
Talc	2	2	2	2	2	2
Total	200	200	200	200	200	200

II. RESULTS AND DISCUSSIONS

- **Preformulation study of drug.**

1. Organoleptic properties:-The drug sample was found to be white, smooth powder.

2. Melting point :-The melting point was found to be in the range of 143-145°c.

3. Determination of λ max:-The UV absorption spectrum of Enalapril was determined in the phosphate buffer pH 6.8 as shown in Fig. 1. The maximum absorbance of Enalapril at 205nm.

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Fig. 1: UV spectrum of Enalapril.

4. Calibration curve of Enalapril in phosphate buffer (pH 6.8)

Table no. 6: Calibration Curve of Enalapril and its absorbance in phosphate buffer pH 6.8 at 205nm.

Sr. No.	Concentration (µg/ml)	Absorbance at 205 nm
		6.8 pH phosphate buffer
0	0	0.00
1	2	0.O87±0.002
2	4	0.189±0.001
3	6	0.26±0.003
4	8	0.350±0.005
5	10	0.441±0.006

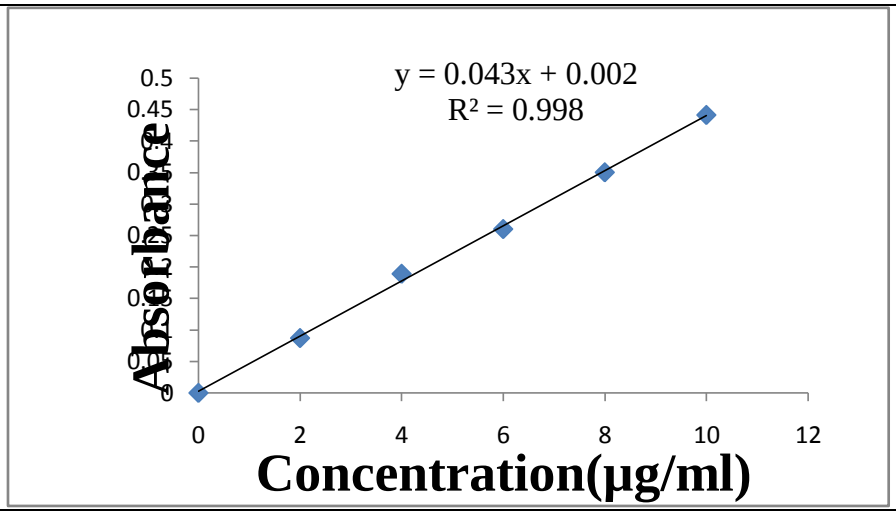

Fig.2: Calibration Curve of Enalapril at 205nm in phosphate buffer pH 6.8

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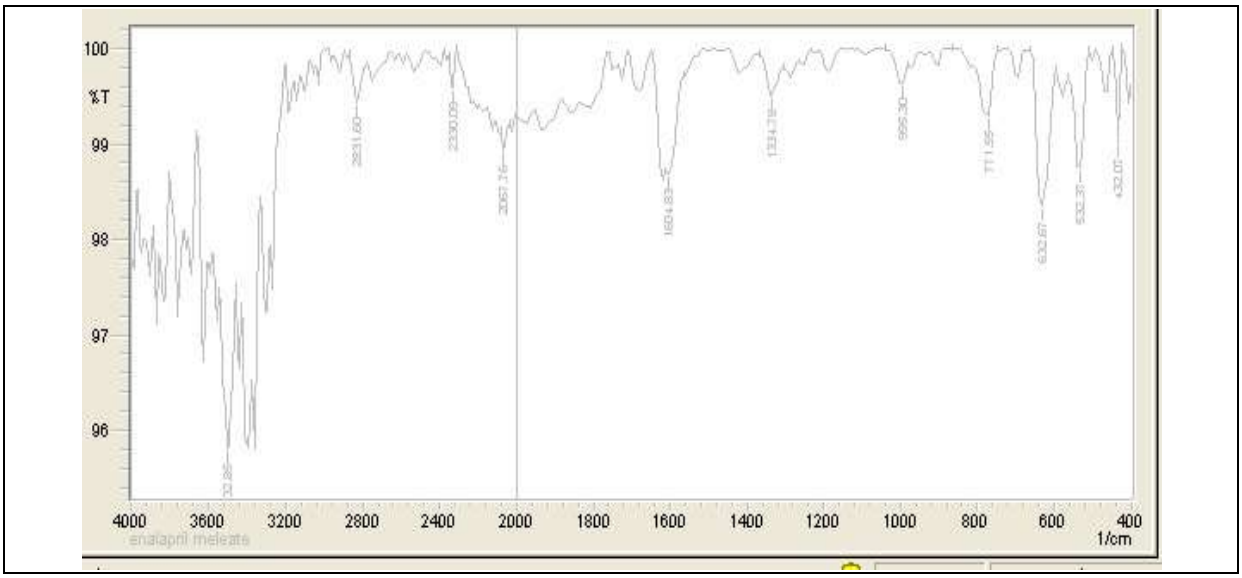

Fig. 3:FTIR of Enalapril

Table no. 7: Interpretation of FTIR spectrum for Enalapril

Functional group	Vibrational Frequencies (cm^{-1})	
	Observed	**Reported**
C-H Stretching	2831	3000-2850
O-H Stretching	2831	3300-2500
C=O Stretching	1725	1760-1690
N-H Bending	1604	1650-1580
C-O Stretching	1225	1320-1000

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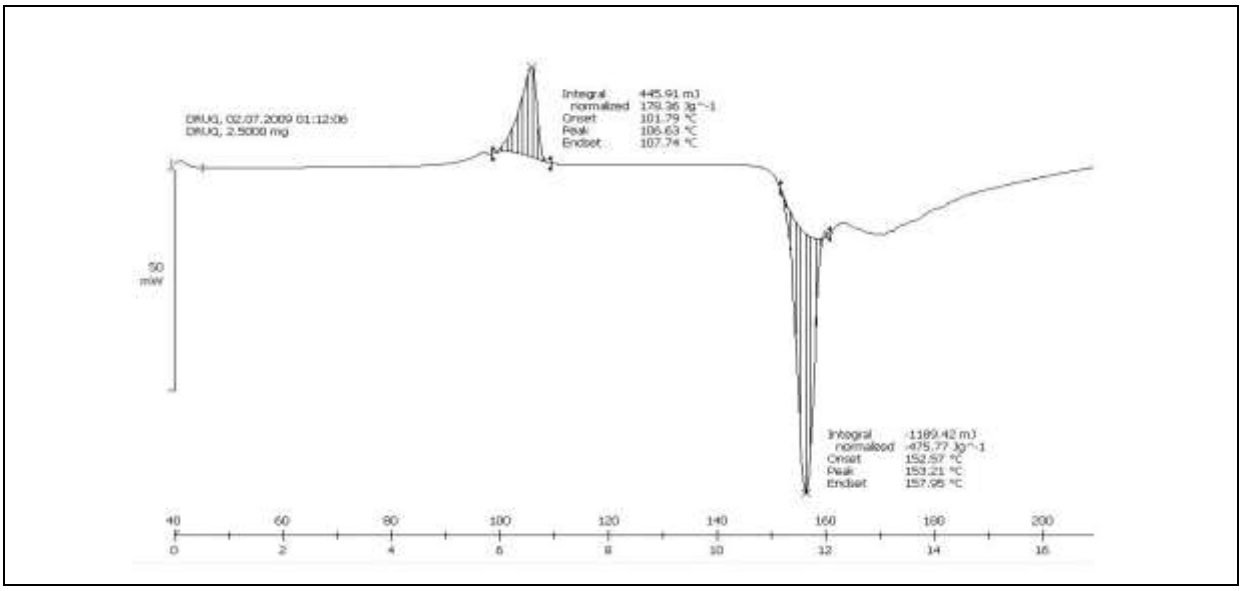

Fig.4: DSC of Enalapril maleate . (Peak = 153.21°c)

Exothermic peak =106.63 °c

Preformulation study of polymers

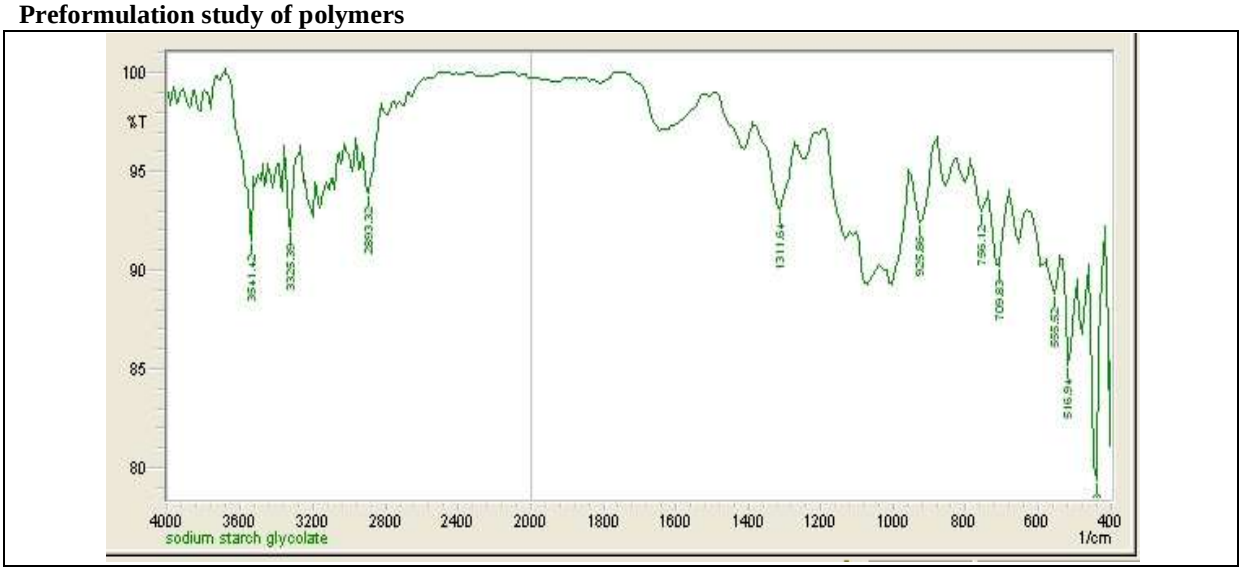

Fig.5 : FTIR Spectrum of Sodium starch glycolate

Table no. 8: Interpretation of FTIR spectrum for Sodium starch glycolate

Functional group	Vibrational Frequencies (cm^{-1})	
	Observed	**Reported**
O-H Stretching	2893	3300-2500

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C-H Stretching	3325	3330-3270
C-H Stretching	2893	3000-2850
C-O Stretching	1311	1320-1000

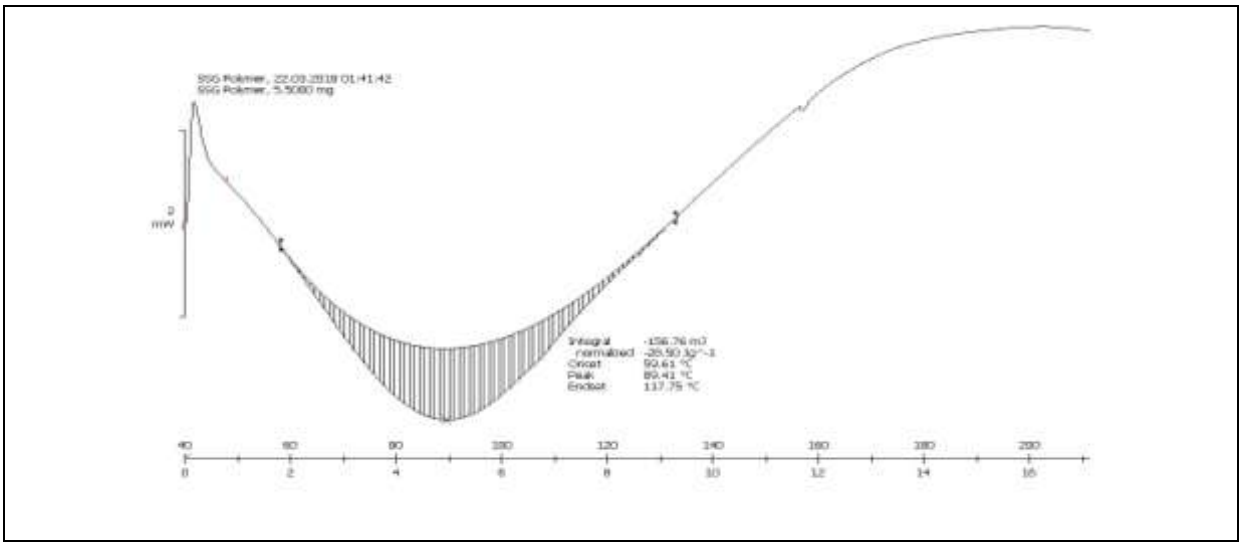

Fig.6 : DSC thermogram of Sodium starch glycolate. (peak= 89.41 °c)

Drug-polymer compatibility studies

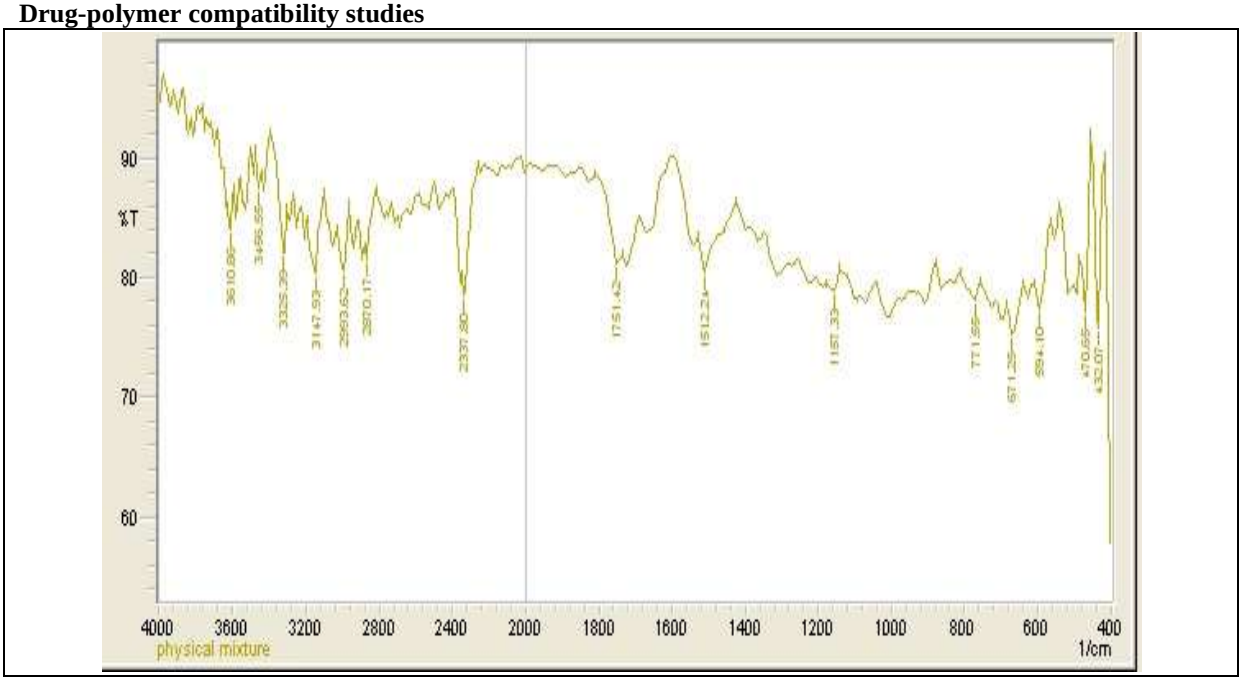

Fig.9: FTIR spectrum for physical Mixture of Drug, sodium starch glycolate and guar gum.

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Table no.10: Interpretation of FTIR Spectrum Values for Physical Mixture .

Functional group	Vibrational Frequencies (cm^{-1})	
	Observed	**Reported**
C-H Stretching	2993	3000-2850
O-H Stretching	3147	3300-2500
N-H Bending	1604	1650-1580
C=O Stretching	1751	1760-1690
C-O Stretching	1157	3200-1000

Formulation of fast dissolving tablets of Enalapril.

Table no.11: Composition of fast dissolving tablets of Enalapril.

Ingredient(mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Enalapril maleate	10	10	10	10	10	10
Sodium starch glycolate	-	-	-	2	4	6
Guar gum	2	4	6	-	-	-
Microcrystalline cellulose	100	100	100	100	100	100
Mannitol	84	82	80	84	82	80
Magnesium stearate	2	2	2	2	2	2
Talc	2	2	2	2	2	2
Total	200	200	200	200	200	200

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Micromeritic Properties:

Table no.12: Observation table of Micromeritic Properties of FDTs

Batch code	Angle of repose (Degree)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	28.19±1.20	0.283±0.001	0.324±0.003	12.66±0.01	1.14±0.005
F2	29.76±0.90	0.294±0.0005	0.339±0.006	13.38±0.44	1.15±0.04
F3	28.44±1.10	0.298±0.002	0.350±0.001	15.37±0.45	1.17±0.02
F4	28.84±0.80	0.29±0.001	0.334±0.003	13.29±0.37	1.15±0.005
F5	29.89±0.40	0.291±0.003	0.340±0.002	14.46±0.06	1.16±0.04
F6	28.16±1.30	0.287±0.002	0.335±0	14.22±0.10	1.16±0.02

(Mean±SD; n = 3)

Evaluation of FDTs tablets

Table no.13: Post compression study of prepared fast dissolving tablets.

Batch	Hardness kg/ cm^2	Thickness (mm)	Diameter (mm	Friability (%)	Weight variation (%) ±S.D
F1	3.26±0.30	3.22±0.30	8.060±0.048	0.79	198±1.74
F2	3.4±0.20	3.24±0.2	8.06±0.008	0.76	198±1.52
F3	3.22±0.50	3.30±0.50	8.08±0.014	0.92	198±1.42
F4	3.4±0.4	3.34±0.46	8.10±0.009	0.99	199±2.17
F5	3.46±0.41	3.33±0.11	8.057±0.004	0.66	200±2.38
F6	3.68±0.10	3.32±0.08	8.07±0.004	0.73	200±1.98

(Mean±SD; n = 3)

Table no.14: Post compression study of prepared Fast dissolving tablets:

Batch	Drug content (%)	Wetting time (seconds)	Water absorption ratio	Disintegration time (seconds
F1	99.05±0.0471	64±1.559	18.71±0.578	78±2.449
F2	91.70±0.150	63±1.699	18.42±0.769	75±5.792
F3	96.14±0.179	60±1.632	14.77±1.153	68±2.449
F4	96.03±0.285	35±3.265	17.34±1.871	50±3.741

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F5	98.46±0.233	33±2.943	16.02±1.132	46±2.054
F6	99.16±0.203	22±1.885	14.77±1.153	42±2.054

In-vitro drug release from Enalapril FDTs

Table no. 15: In-vitro drug release data from prepared fast dissolving tablets.

Time (min)	**Batch**					
	Percentage cumulative drug release \					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	37.45	35.78	42.79	34.09	37.86	43.25
10	50.67	46.98	50.32	41.92	48.96	65.98
15	70.87	60.27	63.52	65.81	53.32	75.16
30	85.23	75.82	79.98	85.30	75.01	79.98
45	90.89	89.12	92.17	90.08	87.19	91.23
60	95.45	93.98	95.88	95.98	90.65	97.98

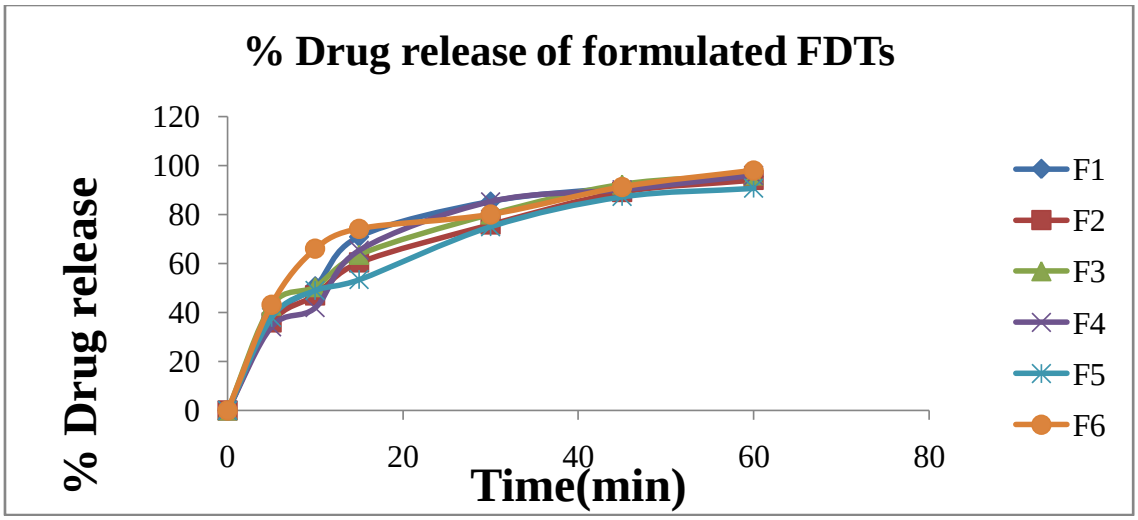

Fig.10.: Cumulative % Drug release from FDTs Formulations.

- The in- vitro dissolution studies were performed on all prepared FDTs using phosphate buffer pH 6.8 to drug release was measured at various interval time and results were given in Table no.15
- The maximum % drug releases of Enalapril from prepared FDTs using Sodium starch glycolate and Guar gum were found 97.98% and 95.88% respectively at the end of 60 min.
- Thus the dissolution rate of FDT was found higher with Sodium starch glycolate than the Guar gum.
- Amongst the various FDT formulations, tablets of batch F6 prepared with Sodium starch glycolate at 3% w/w concentration showed complete release of drug within 60 min. And hence F6 formulation came out to be the best formulation among the others.

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- **Characterization of FDTs**
- **FTIR of formulation F6 by direct compression method with Sodium starch glycolate:**

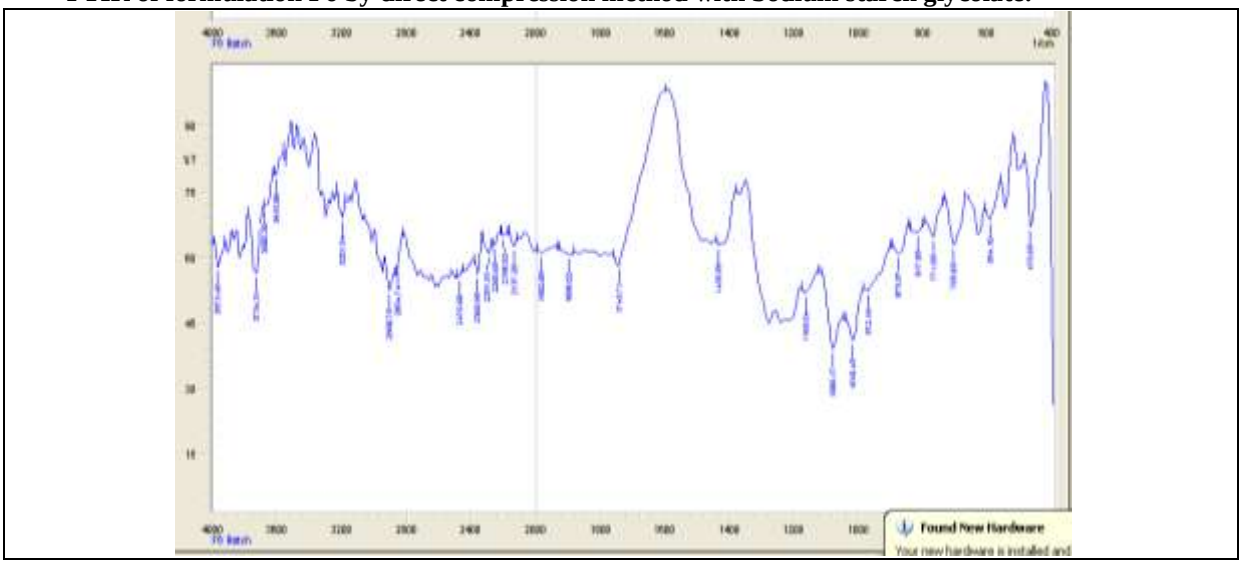

Fig.11 : FTIR spectrum of formulation F6

Table no16 : Functional group with their vibrational frequencies of FTIR spectrum of Formulation F6.

Functional group	Vibrational frequencies(cm^{-1})	
	Observed	**Reported**
C-H stretching	2908	3000-2850
O-H stretching	2908	3300-2500
O-H stretching	3201	3500-3200
C=O stretching	1743	1760-1690
C-O stretching of esters	1743	1750-1735
C-C stretching	1435	1500-1400
C-O stretching	1165	1320-1000

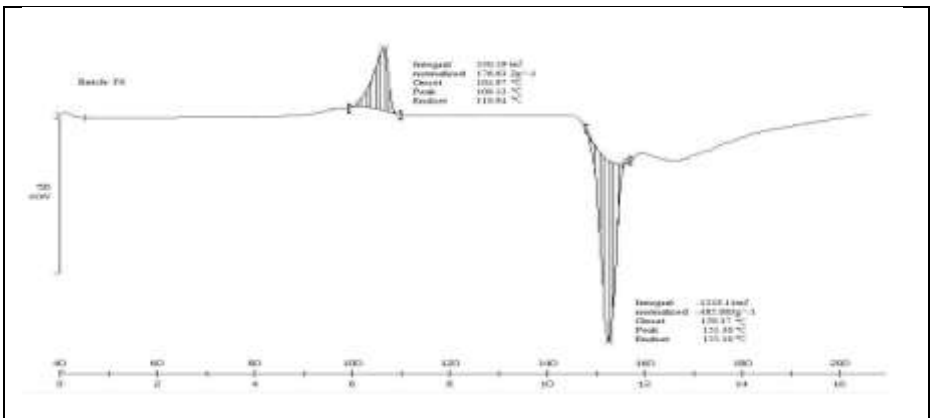

Fig.12: DSC thermograph of formulation F6 exothermic peak at 109.12 ^{0} C & peak=151.30 ^{0} C.

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Stability study

Table no.17: Drug content and disintegration time after stability study

Batch	Drug content (%)before stability study	Drug content (%)after stability study	Disintegration time(sec) before stability study	Disintegration time (sec) after stability study
F1	99.05±0.0471	99.12±0.0510	78±2.449	78±2.443
F2	91.70±0.150	92.00±0.162	75±5.792	74±5.782
F3	96.14±0.179	96.72±0.142	68±2.449	67±2.409
F4	96.03±0.285	96.00±0.172	50±3.741	50±3.732
F5	98.46±0.233	98.50±0.201	46±2.054	46±2.154
F6	99.16±0.203	99.20±0.202	42±2.054	42±2.254

III. CONCLUSION

- Fast dissolving tablets of Enalapril were prepared by varying concentration of sodium starch glycolate and guar gum. FDTs were prepared by direct compression technique.
- Preformulation study on drug and polymer revealed that there was no interaction between drug and polymer.
- All the formulations were evaluated for Drug content uniformity, Disintegration test, IR, DSC, stability study and in-vitro drug release.
- All the designed formulations of fast dissolving tablets of Enalapril showed faster disintegration time from F4 to F6 batch due to increase in concentration of sodium starch glycolate.
- The FTIR and DSC studies indicated that there was no interaction between drug and polymer.
- In-vitro drug release studies were carried out in phosphate buffer pH 6.8.
- From stability studies of selected formulation, it was found that formulation was stable for 45 days. The FDTs did not show any significant change in drug content and disintegration time at the end of 45 days.
- Among prepared formulations of FDTs of Enalapril, tablets from batch F6, prepared using 3 % w/w of Sodium starch glycolate showed faster disintegration time of 42±2.054 seconds and complete release of drug within 60 min and higher drug content which was 99.16±0.203%.
- As a result of this study, it was concluded that the direct compression method is suitable for formulation of fast dissolving tablets to improve the disintegration time and drug dissolution rate and subsequently bioavailability and onset of action of Enalapril.

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