WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 8, Issue 1, 295-304. Research Article ISSN 2277– 7105

FORMULATION AND OPTIMIZATION OF FAST DISSOLVING TABLETS OF OLMESARTAN

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Article Received on
14 Nov. 2018,
Revised on 04 Dec. 2018,
Accepted on 24 Dec. 2018
DOI: 10.20959/wjpr20191-13930

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ABSTRACT

The objective of the present study was to prepare fast disintegrating tablets of olmesartan with sufficient mechanical integrity to achieve faster disintegration for patient convenience. The tablets were prepared by direct compression method using superdisintegrants using sodium starch glycolate, cross carmellose sodium and cross povidone at 1, 1.2% level for F1 to F6 formulations and sodium bicarbonate at 1.8, 2, 2.2% levels, and citric acid at 0.2, 0.3%, 0.5% level. The tablets were evaluated for hardness, friability, disintegration, uniformity of drug content and dispersible time. They were found to be within I.P. limits. The drug content of all tablets were found to be 98.3 – 100.2%. FT-IR shows no interaction between drug and polymer. It was concluded that, the formulation F6 was found to be optimizing formulation having disintegration time 29 seconds and % of drug release 98.58% at the end of 10 min.

KEYWORDS: Olmesartan, Super disintegrate, Fast Dissolving, Cross Carmellose.

INTRODUCTION

Fast dissolving drug delivery is rapidly gaining acceptance as an important new drug delivery technology. These dosage form dissolve or disintegrate in oral cavity within a minute even without need of water or chewing, usually super disintegrants are added in formulation to facilitate break-up and disintegrate rapidly in to smaller particles. The oral route of drug administration is the most common and preferred method of delivery due to convenience and ease of Administration. From a patient's perspective, swallowing a dosage form is a comfortable and a familiar means of taking medication. Although the oral route of administration is preferred, for many drugs it can be a problematic and in efficient mode of delivery for a number of reasons. Limited drug absorption resulting in poor bioavailability is

paramount amongst the potential problems that can be encountered when delivering an active agent via the oral route. The need for non- invasive drug delivery systems continues due to patient's poor acceptance and compliance with existing delivery regimes, limited market size for drug companies and drug uses coupled with high cost of disease management. ODT is one such dosage form which is useful for, geriatric patients mainly suffering from conditions like hand tremors and dysphasia. Pediatric patients who are unable to swallow easily because their central nervous system and internal muscles are not developed completely. Traveling patients suffering from motion sickness and diarrhoea that do not have easy access to water. Patients with persistent nausea for a long period of time are unable to swallow. The enhancement of solubility and dissolution rate of poorly water soluble drugs remains one of the most challenging aspects of drug development. Several approaches have been followed in improving solubility of such drugs. In the present investigation, olmesartan was selected as a drug candidate for developing Fast dissolving drug delivery system. Olmesartan is the angiotensin II receptor blocker used for the treatment of hypertension. It is white to light yellowish-white powder or crystalline powder. It is practically insoluble in water and sparingly soluble in methanol It is well absorbed by oral route and used in hypertension. Its oral bioavailabiity is 26% and having 99% plasma proteins binding. It is metabolized in liver. Elimination half -life of olmesartan is 13 hrs.

Formulation of Dispersible Tablets of Olmesartan

Table No. 1: Formulation of dispersible tablets of olmesartan.

S.No	Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Olmesartan	20	20	20	20	20	20	20	20	20
2	Sodium starch glycolate	10	10	-	-	-	-	-	-	-
3	Croscarmellose sodium	-	-	10	12	-	-	-	-	-
4	Crospovidone	-	-	-	-	10	12	-	-	-
4	Sodium bi carbonate	-	-	-	-	-	-	18	20	22
5	Citric Acid	-	-	-	-	-	-	2	3	5
06	Mannitol	67	65	67	65	67	65	57	54	50
7	Aspartame	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
8	Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
	TOTAL (mg)	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

RESULTS AND DISCUSSION

Olmesartan standard calibration curve

Serial of dilutions are made from standard working solution with distilled water to get concentration from 10 to 50 microgram/ml and the absorbance was measured at 255nm.

Table No. 2: Olmesartan standard calibration curve.

S.No	Concentration (mcg/ml)	Absorbance
1	10	0.114
2	20	0.226
3	30	0.352
4	40	0.470
5	50	0.582

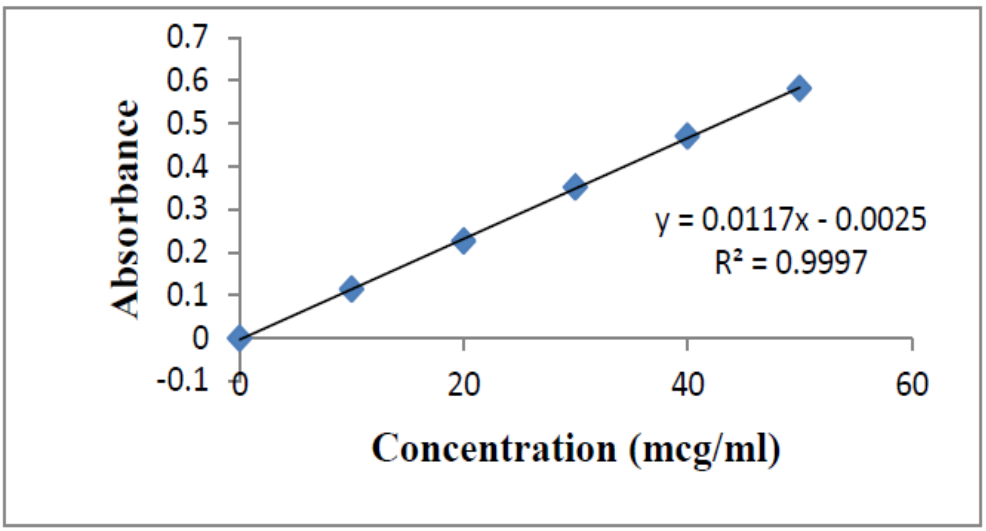

Figure 1: Standard graph of Olmesartan.

Micromeritic Properties to the Olmesartan

Table No. 3: Micromeritic properties to the olmesartan.

Form. No	Bulk density (gm/cm3)*	Tapped density (gm/cm3)*	Compressibility Index (%)*	Hausner Ratio*	Angle of repose (θ°)*
F1	0.425±0.002	0.464±0.001	8.60±0.002	1.094±0.002	23.21±0.035
F2	0.416±0.001	0.459±0.004	9.36±0.002	1.103±0.001	24.29±1.28
F3	0.425±0.001	0.465±0.001	8.60±0.004	1.094±0.003	30.31±0.350
F4	0.421±0.002	0.459±0.002	8.27±0.006	1.090±0.005	27.21±0.330
F5	0.431±0.003	0.470±0.007	9.57±0.002	1.105±0.002	26.26±0.426
F6	0.425±0.001	0.481±0.003	10.60±0.004	1.118±0.005	31.78±0.203
F7	0.401±0.004	0.462±0.002	9.5±0.002	1.201±0.007	24.48±0.801
F8	0.412±0.003	0.458±0.004	9.06±0.002	1.082±0.002	35.72±0.720
F9	0.419±0.007	0.424±0.001	8.07±0.007	1.063±0.004	23.78±0.210

The Bulk density of various powder mixed blends prepared with different super disintegrants, was measured by graduated cylinder. The bulk density was found in the range 0.401– 0.431 kg/cm^3.

The Tapped density of various powder mixed blends prepared with different super disintegrants, was measured by graduated cylinder. The Tapped density was found in the range 0.424 – 0.481 gm/cm^3.

The Compressibility index of various powder mixed blends, prepared with different super disintegrants, using bulk density and tapped density data, compressibility index was calculated. It was found in the range 8.07 – 10.60%.

The Hausner's ratio of various powder mixed blends, prepared with different super disintegrants, using bulk density and tapped density data, Hausner's ratio was calculated. It was found in the range 1.082 – 1.201.

Angle of repose ranged from 23.21to 35.72. The flow properties of powder blend in all formulations exhibit good flow characteristics.

Assay of Prepared Olmesartan Tablets

Table No. 4: Assay of prepared Olmesartan tablets.

Formulation No	**Assay of in % w/w**
F1	98.3
F2	98.6
F3	99.0
F4	101.7
F5	101.5
F6	102.2
F7	99.03
F8	98.12
F9	100.02

Tablets were evaluated by using assay method. The drug was obtained in the acceptable limit. The drug content was found in the range **98.3 – 102.2%.**

In–vitro drug release studies

Comparative Dissolution Profile of Olmesartan dispersible tablets in 0.1 HCL Buffer Solution.

Table no. 5: Average % Drug Release at 10 Minutes.

Time in min	F1	F2	F3	F4	F5	F6	F7	5F8	F9
0	0	0	0	0	0	0	0	0	0
2	56.13	61.05	66.2	68.41	69.53	75.23	70.16	65.28	69.16
4	65.12	72.12	73.12	76.45	78.25	85.56	79.57	72.21	78.43
6	78.21	80.45	86.45	80.47	82.32	90.45	82.78	89.49	84.75
8	85.17	91.56	91.56	88.96	90.75	96.21	90.56	89.46	89.42
10	89.88	92.75	96.45	94.15	94.78	98.58	91.45	94.75	95.45

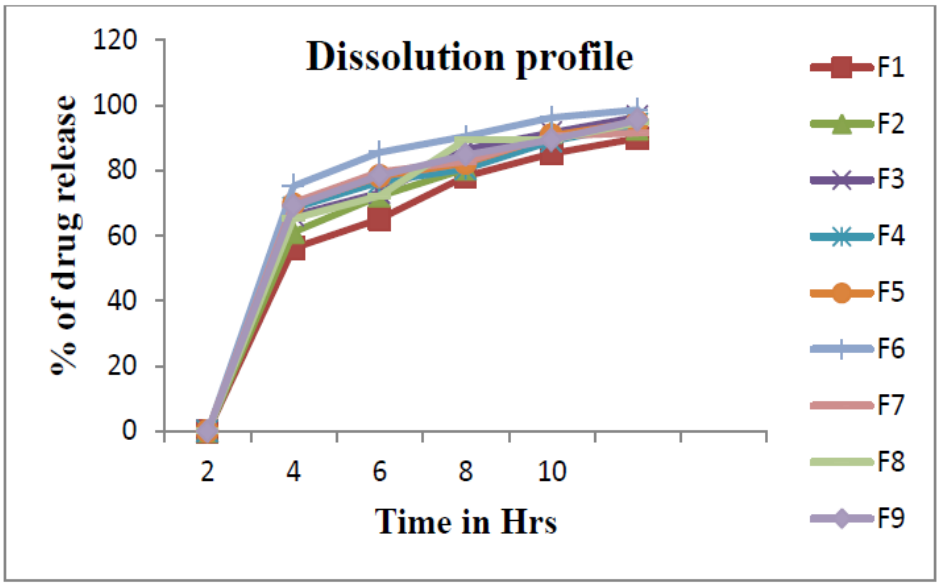

Figure 2: Graph of Olmesartan % Drug Release.

In-vitro drug release studies were conducted for the formulation using USP dissolution apparatus type-II (paddle), at 25 rpm. The percentage drug release at the end of 10 min was found in the range **89 – 98%.**

Kinetics study

Table 6: Dissolution Kinetics of optimized batch F6.

Time	Square root of time	Log time	% drug released	Log % drug released	% drug remaining	Log % drug remaining
0	0	-	0	-	100	2
2	1.414214	0.30103	75.23	1.8763911	24.77	1.393926007
4	2	0.60206	85.56	1.9322708	14.44	1.159567193
6	2.44949	0.778151	90.45	1.9564086	9.55	0.980003372
8	2.828427	0.90309	96.21	1.9832202	3.79	0.57863921
10	3.162278	1	98.58	1.9937888	1.42	0.152288344

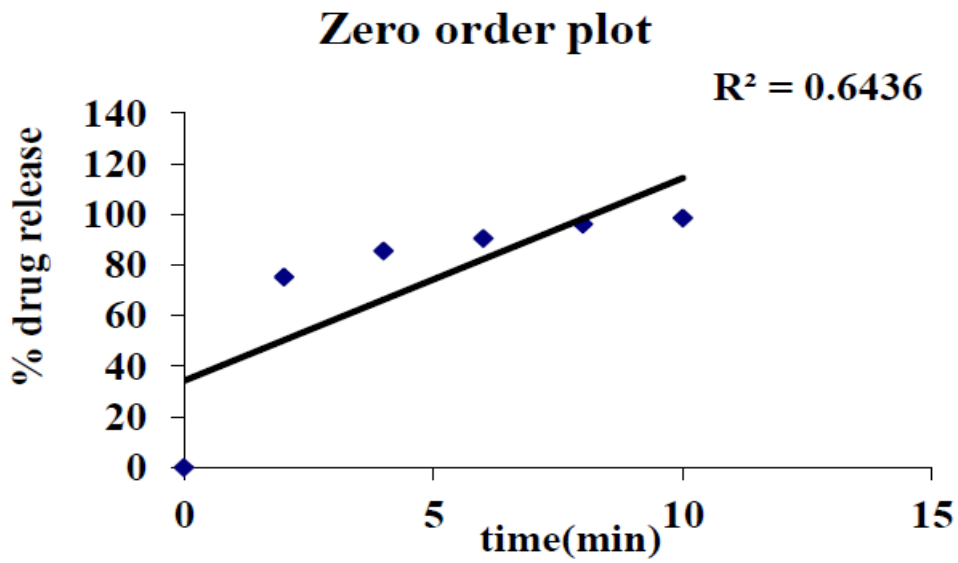

Figure No. 3: Zero order Kinetics of optimized batch F6.

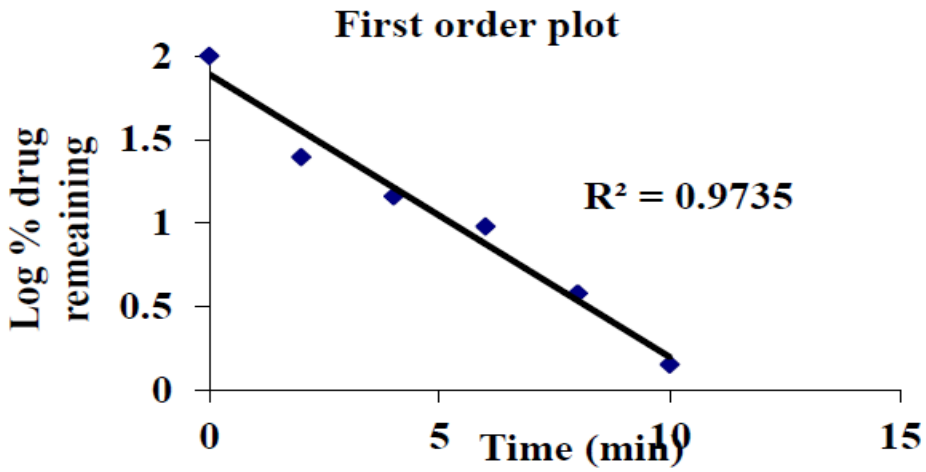

Figure No. 4: First order Kinetics of optimized batch F6.

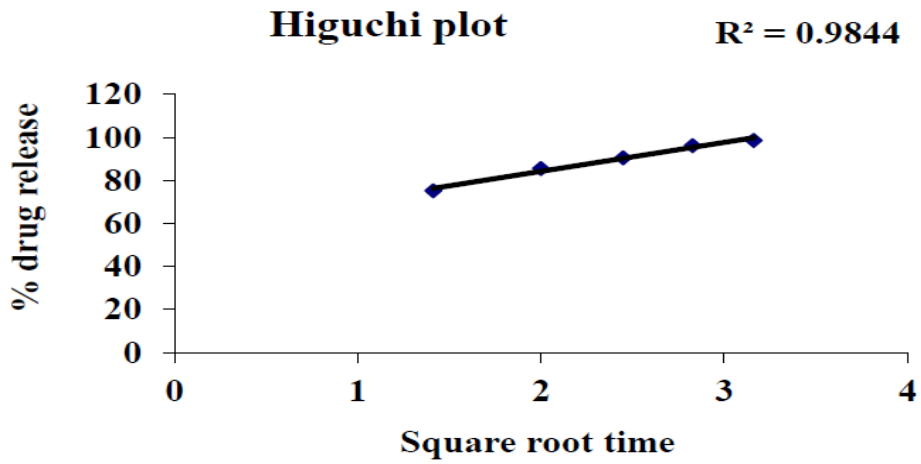

Figure No. 5: Higuchi Kinetics of optimized batch F6.

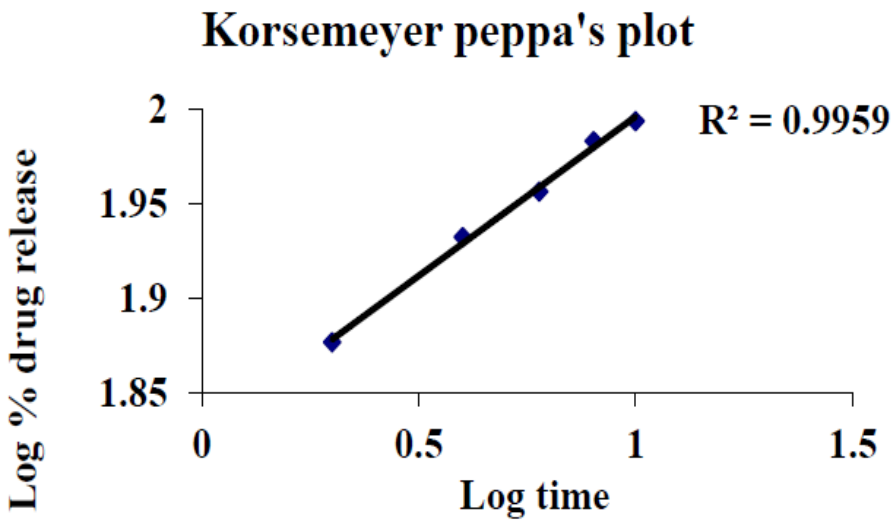

Figure No. 6: Korsemeyer Kinetics of optimized batch F6.

DISCUSSION

The release profile of the optimized formula F6 fitted best to Korsmeyer-Peppa's model with R^2 value of 0.995. As the n value for the Korsmeyer-Peppas model was found to be greater than 1, it follows case-2 transport.

FTIR studies

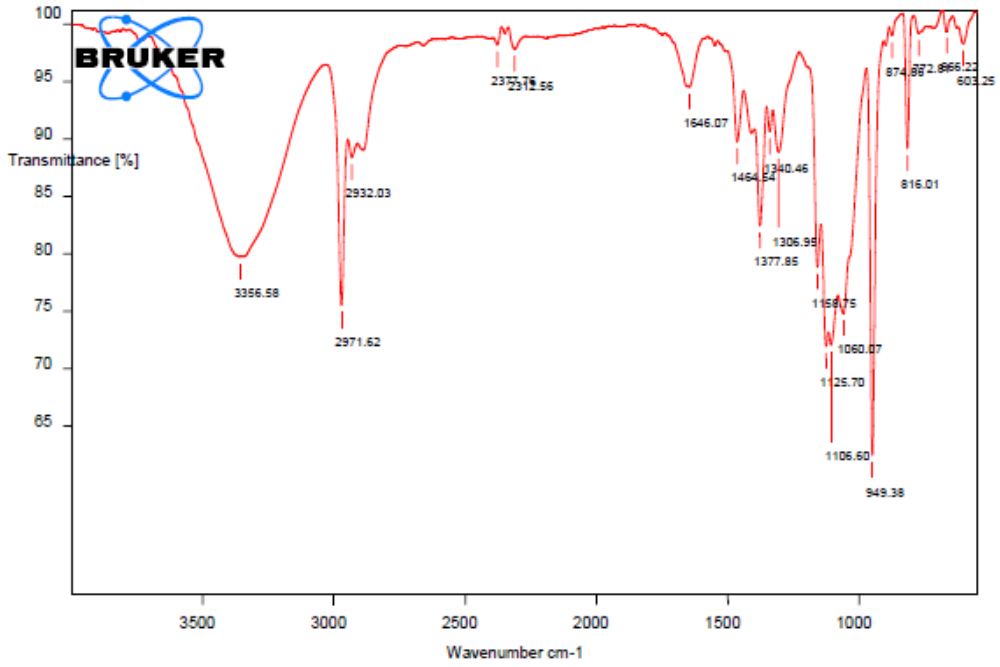

Figure No 7: Infra-Red Spectrum of Pure Olmesartan.

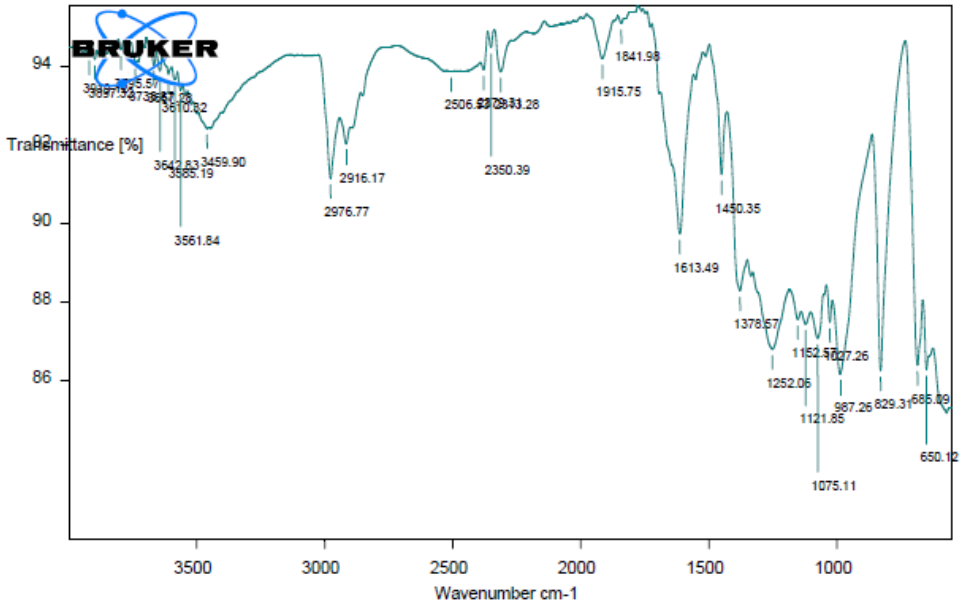

Figure No 7: Infra-red spectrum of pure drug with optimized formulation F6.

From the above figures, it can be seen that, the major functional group peaks observed in spectra of Drug with all the polymers remains unchanged as compared with spectra of **Olmesartan**. So from the above IR spectra it can be observed that there is no interaction between **Olmesartan** and Polymers used in the formulations.

SUMMARY AND CONCLUSION

The study was carried to formulate and evaluate dispersible tablet dosage form containing Olmesartan a Anti-hypertensive drug.

The present study is an attempt to select best possible combination of diluents and disintegrants to formulate dispersible tablet of Olmesartan which disintegrates within few minutes thereby reducing the time of onset of action.

Mannitol is selected as diluents, Sodium starch glycolate, Crosspovidone, croscarmellose sodium were selected as super disintegrants. Microcrystalline cellulose was used in all formulations in different concentrations. Aspartame as a sweetening agent, Magnesium stearate as Lubricant and Talc as glidant.

Sodium starch glycolate is used as the super disintegrant in the formulation F1 – F2 at the concentrations of the 0.5, 0.5% respectively.

Cross carmellose sodium is used as the super disintegrant in the formulation F3 – F4 at the concentrations of 0.5, 0.6% respectively.

Crosspovidone is used as the super disintegrant in the formulation F5 – F6 at the concentrations of 0.5, 0.6% respectively.

Sodium bicarbonate and Citric Acid is used as the super disintegrant in the formulation F7 – F9 at the concentrations of 0.9, 1, 1.2% and 0.1, 0.15, 0.25 respectively.

- Direct Compression method was used to formulate the tablets.
- All the formulations were showed the acceptable flow properties and the precompression parameters like Bulk density, Tapped density and Hausner ratio.
- The post compression parameters like Hardness, Friability, Disintegration time, Weight variation, wetting time, Dispersion time values were found to be within the IP limits.
- The percentage Drug content of all tablets was found to be between 98.3% - 100.2% of Olmesartan, which is within the limit.

As the concentrations of the Crosspovidone increases in the formulations F5 – F6 the disintegration time found to be decreased and the disintegration time for these formulations were 34.85, 29.25 seconds respectively and the percentage drug release was also found to be increased for these formulations as 94.78, 98.58% respectively. From the above results it was found that as the concentration of Crosspovidone increased and mannitol decreases the disintegration and dissolution time was found to be improved, so considering the above results it was found that the F6 batch was found to be optimized batch and it pass all the preformulation parameters and evaluation results as per the IP limits

From the data obtained, it is observed from the formulation containing Crosspovidone - 12mg, mannitol - 65mg in Formulation F6, shows Disintegration time in 29 seconds and the Percentage drug release is of 98.58% at the end of 10 min which satisfied all the tablet evaluation parameters for dispersible tablet. Hence looking at all the satisfactory parameters F6 batch is selected as the optimized batch.

CONCLUSION

From the data obtained, it is observed from the formulation containing Crosspovidone - 12mg, mannitol 65mg in Formulation F6, shows Disintegration time in 29 seconds and the

Percentage drug release is of 98.58% at the end of 10 min which satisfied all the tablet evaluation parameters for dispersible tablet.

REFERENCES

1. Leon Lachman, Herbert A. Lieberman, Joseph L. Kaing, "The theory and practice of industrial pharmacy", third edition. (Page No.293, 294, 296, 311- 319).
2. Howard C. Ansell's, Loyd V. Allen, jr. and Nicholas G. Poporich, in; "Pharmaceutical Dosage forms and Drug Delivery System", seventh edition, Lippincott Williams and Wilikins, Philadelphia, 1999 (Page No. 203-209).
3. Michele Danish and Mary Kathryn Kottke., In; Gilbert S Banker and Christopher T. Rhodes., Eds., "Modern pharmaceutics", third edition, Marcel Dekker, Inc, New-York, 1996 (Page No.830).
4. V L Allen, G N Popavich, C H Ansel, In; Ansel's pharmaceutical Dosage Forms and Drug Delivery systems, 8th edition, BI publications, 2006.
5. YW Chien. Novel drug delivery systems. In: Novel drug delivery systems. Edn 2, Marcel Dekker, New York, 1992; 193-196.
6. S Rawat, SK Jain, Eur. J. Pharm. Biopharm., 2004; 57: 263-267.
7. H Sohi, Y Sutana Y, R Khar, Drug Dev Ind Pharm., 2004; 30: 429-448.
8. Bhatt, Priyal, R Patel, Int J Pharm Pharm Sci, 2011; 3(5): 1-6.
9. SB Bhanja, P Ellaiah, BS Nayak, DK Mahapatra, BB Panigrahi. Inter J Pharml Tech., 2011; 3(3): 2961 - 2991.
10. V Bhardwaj, M Bansal, PK Sharma. Am Eurasian J Agric Environ Sci, 2010; 5(4): 264-269.