World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Published by Atom and Cell Publishers
Available online at: http://www.wjpsonline.org/
Original Article

Development and *in vitro* evaluation of fast dissolving films of levocetirizine dihydrochloride

Aastha Shrestha, Pradeep Paudel, Shrawani Lamichhane, Srijan Shrestha, Junu Khatri Silwal and Bhupendra Kumar Poudel

National Model College for Advance Learning, Tribhuvan University, Nepal

Received: 08-09-2014 / Revised: 21-09-2014 / Accepted: 23-09-2014

Abstract

The study attempts to design oral dispersible film of Levocetirizine dihydrochloride by solvent casting method. The films were made in such a way that each 2X2 cm^2 of film contains 5mg of Levocetirizine. The preliminary 10 batches were formulated for designing the Oral dispersible film wherein the effects of plasticizer, effectiveness of CCS and CP; and concentration of HPMC were assessed on the characteristics of the films. Then design, characterization, optimization and evaluation of film using Box Behnken design was used to investigate the influence of independent factors, i.e. content of HPMC-15 cps, PEG and Crospovidone on response variable, i.e. disintegration time. When target of 22 seconds DT is made, the combination of the three variables should be such that HPMC should be used at around 35% w/w, CP at around 4% w/w and PEG should be used at around 10% v/w. Further, from the study it was found that HPMC had increasing effect in DT while, crospovidone and PEG had decreasing effect. Thus, it can be concluded that oral dispersible film of Levocetirizinedihydrochloride for quick relief from allergic rhinitis can be made by using HPMC as polymer using solvent casting method.

Keywords: Levocetirizine dihydrochloride, films, DT, HPMC, solvent casting

INTRODUCTION

Oral Fast Dissolving Films (OFDFs) are the delivery system which consists of a very thin oral strip, which is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates and dissolves to release the medication for oromucosal absorption or with formula modifications, will maintain quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed [1]. This technique is one such novel approach to increase consumer acceptance by virtue of rapid dissolving, self-administration without water or chewing [2]. Fast dissolving oral delivery film is most acceptable and accurate oral dosage form which bypasses the hepatic system and shows more therapeutic response. It combines all the advantages of tablet (accurate dose, self-administration) with those of liquid dosage forms (easy swallowing, quick bioavailability) and its one of the disadvantages being that high dose cannot be incorporated into the strips [3]. Despite the advances in FDT technologies, there are still many aspects to improve and problems waiting to be solved in the FDT formulations. Formulations of hydrophobic drugs are still a challenge, especially when the amount of drug is high, as the dose increases; the formulation sacrifices its fast disintegrating property. The disintegration times of most FDTs on the market are acceptable but certainly there is a room for improvement as the disintegration time is related to other formulation variables [4]. ODTs may disintegrate in most conditions and thus there is always a probability of deterioration of the prepared tablets unless the packaging of the formulation is considered with highest care. And with the other large no. of advantages associated with it, this is a very small price to pay. Moreover those drugs that require sustained release are not good candidates to be formulated as ODTs. These disadvantages may limit the preparation of ODTs in some cases [5]. The ideal characteristic of drug selected for its formulation into films should have a pleasant taste, small or moderate Molecular weight, should have a low dose up to 40mgs. The drug should have good stability and solubility in water as well as in saliva. It should be partially unionized at the pH of oral

***Corresponding Author Address: Aastha Shrestha,** National Model College for Advance Learning, Tribhuvan University, NEPAL*
***E-mail:**aastha803@gmail.com*

cavity and should have an ability to permeate oral mucosal tissue [6]. Fast dissolving films could be formulated with the easily available components such as HPMC, HPC and Sodium Alginate.

MATERIALS AND METHODS

Materials: The drug molecule Levocetirizine dihydrochloridewas received as gift sample from Lomus Pharmaceuticals Pvt. Ltd.Other materials like Crospovidone, HPMC 15 cps, polyethylene glycol400, Tween 80, Aspartame, Citric acid, Glycerol and Mannitol were obtained from Research Laboratory of National Model College for Advance Learning.

Methods: Levocetirizine dihydrochloride fast dissolving films were prepared by solvent casting method. The strips were evaluated for drug content uniformity, film thickness, folding endurance, *in vitro* disintegration time, *in vitro* dissolution studies and surface pH study.

Preparation of cast film containing Levocetrizinde dihydrochloride: Levocetirizine films were prepared by solvent casting technique according to a standard scheme represented by flow chart. First the water soluble polymers were dissolved in water and the drug along with other excipients was dissolved in water, then both the solution were mixed and stirred. PH was adjusted with citric acid to around 7. The solution was coated on glass petri plates and placed in hot air oven for drying. The resultant films were cut into the dimension of 2×2 cm^2 in size. The amount of drug added was calculated based on area of plates so that each dosage (2×2 cm^2) consisted of 5mg of Levocetirizine dihydrochloride.

Optimization of the formulation using Box-Behnken Design: Box- Behnken Design is a type of response surface methodology (RSM) design available for statistical optimization of formulation. Effects of combination of three factors viz, polymer, superdisintegrant and plasticizer in formulation were formulated by Box- Behnken Design. The traditional approach to developing a formulation is to change one variable at a time. By this method it is difficult to develop an optimized formulation, as the method reveals nothing about the interactions among the variables. Hence, Box-Behnken Design with 3 factors and 15 runs were selected for the optimization study.

Evaluation of OFDFs of Levocetirizine dihydrochloride: Pharmacopoeias give the monographs of common dosage forms. Even though dosage form for application in the oral cavity such as medicated chewing gums, oromucosal preparations, orodispersible tablets or oral lyophilisates are included, monographs and specifications for oral films have not yet been established. There are inadequate pharmaceutical technical procedures for analysis in development and quality control of oral films as well. For instance, dissolution and disintegration procedures may be provided, but recommended condition such as volumes of media do not reflect natural conditions in the oral cavity [7].

Following parameters are considered for evaluation of the Levocetirizine dispersible films:

- Weight variation
- Thickness
- Folding endurance
- Surface pH
- In vitro disintegration
- In vivo dissolution
- Uniformity of content

Weight variation: This test ensures the uniformity of the film formed. Ten films each of 2×2 cm^2 area is cut and weighed individually and compared with the average weight for deviation[7].

Thickness: Thickness of film is directly in concern with drug content uniformity so it is necessary to ascertain uniformity in thickness of the film. The thickness test can be carried out by using an electronic micrometer or calibrated digital vernier caliper at five different strategic locations including the measurements at the center and the four corners. Samples with air bubbles, nicks or tears and having mean thickness variation of greater than 5% are excluded from the analysis. Standard deviation is calculated [6, 7].

Folding endurance: It is determined manually by repeated folding of the film at the same place till the film breaks. The number of times the film is folded without breaking is computed as the folding endurance value. This test should be performed on six films of size 2×2 $cm^2$of each formulation and mean ±S.D. calculated [1, 6, 7, 8].

Surface pH: Surface pH of films is determined by dissolving a film in 2ml of distilled water and then the pH of the obtained solution was measured by pH meter. The pH range of 6-7 is considered acceptable [9, 10].

In vitro disintegration: *In vitro* disintegration time is determined visually in a glass beaker with 25ml of suitable buffer with swirling every 10 sec. The disintegration time is the time when the film starts to break. Pharmacopoeial disintegration test apparatus may also be used for the study according few journals and disintegration time for oral films

is 5-30 seconds. Although, no official guidance is available for OFDFs [1, 7, 8 and 11].

In vitro dissolution: Dissolution of OFDFs is performed by USP type II apparatus in 900ml of 6.8 phosphate buffer. The temperature of the medium is maintained at 37±0.5˚C and the paddle is set at the rotation speed of 50 rpm. The samples are withdrawn at interval of every 2minutes, for 30minutes i.e. at 2nd, 4th, 6th, 8th, 10th, 20th and 30th min.Many times the dissolution test can be difficult due to tendency of the strip to float onto the dissolution medium when paddle apparatus is employed.Every time 10ml of sample is withdrawn from each vessel, filtered through whatman filter paper and absorbance of each filtrate sample is measured and compared with 5mcg/ml standard solution using UV-Visible spectrophotometer (λ_{max}, 230 nm), phosphate buffer pH 6.8 as blank. [6, 8, and 10].

Uniformity of Content:

Standard solution: Accurately about 50mg of pure Levocetirizine dihydrochloride is taken and weighed and transferred into a 100ml volumetric flask. Then about 50ml of phosphate buffer solution (PBS) (pH 6.8) is added and dissolved with sonication then the volume is made up to 100ml with PBS (pH 6.8). The solution is then filtered. First few ml of the filtrate is discarded. Then 10ml of filtrate is pipette out and diluted up to 100ml with PBS (pH 6.8) so as to get 10 mcg /ml final concentration and again 5ml from the first dilution is pipette out and diluted to 100ml with PBS(pH 6.8) so as to get 5mcg/ml final concentration.

Test solution: One film is dropped into a 100ml volumetric flask. Then about 50ml of PBS (pH 6.8) is added and dissolved with sonication then volume is made up to 100ml with PBS (pH 6.8). The solution is filtered. First few ml of the filtrate is discarded. Then 5 ml of filtrate is pipette out and diluted up to 5 ml with PBS (pH 6.8) so as to get 5mcg /ml final concentration. The absorbance of the final solution of test and standard Levocetirizine dihydrochloride solution were compared at 230 nm using phosphate buffer pH 6.8 as a blank using UV-spectrophotometer [9].

RESULTS AND DISCUSSIONS

As fast dissolving films are intended to have rapid action, rapid disintegration followed by rapid dissolution and absorption is desired. For obtaining such fast release of drug selection of right excipients in right proportion is a must. Hence, preliminary batches were prepared after extensive literature review for the confirmation of excipients and their concentrations that is to be used. As seen from the Table1, crospovidone(CP) was found to be a more effective superdisintegrant than croscarmellose (CCS) while formulating fast dissolving films. The disintegration profile of films was found to improve with the use of CP rather than with the use of CCS. The concentration of other excipients and their concentrations remaining constant, preliminary batch P1 with CP as the superdisintegrant gave a lower disintegration time of 30secs when compared to disintegration time of 130 seconds for the preliminary batch P2 with CCS as the superdisintegrant. So CP was selected as a suitable superdisintegrant for further formulations. HPMC is the film forming polymer and at the same time its concentration as a prominent effect upon the disintegration time of the films. Hence selection of optimum range of HPMC becomes very important. When HPMC was used in concentrations around 20, no proper films were formed. It became very difficult to remove the film from the plate and cut it into desired size. When HPMC was used in concentration range of 35%-40% w/w, better disintegration profile was obtained and also the films formed looked good in appearance and could be easily removed from the plate and cut into required dimensions. When a concentration above 40%w/w was employed, the disintegration time of the films increased significantly. Preliminary batches P2, P3, P6, P7 and P8 disintegrated within one minute while preliminary batches P4 and P5 disintegrated way above one minute. Hence, the concentration range 35%-40% w/w of HPMC was selected. PEG when used as plasticizer in concentration range of 0-15% v/w, allowed the formation of films that looked good in appearance and flexible as well while when the concentration exceeded 15% v/w brittle films were formed. Glycerol was used as humectants, at concentrations above 10% v/w, the films looked over humid, wet and the drying time had to be increased. Considering all these findings, the final optimized batches were designed by the Box-Behnken Design.

Optimization of formulation from Box- Behnken Design: Figure 8 shows that for obtaining the disintegration time below 20 secs, the combination of concentrations of CP and HPMC selected should be such that concentration of HPMC should be around 35% w/w not reaching 36%w/w and concentration of CP should be below 4.6% w/w, concentration of PEG being constant i.e. 10% v/w. The plot also shows different areas representing the combinations of concentrations of CP and HPMC and the respective disintegration times the combinations ma bring about. It also indicates that any combination of concentration of HPMC exceeding 39%w/w and that of CP is less than

4.2%w/w the disintegration time of films exceed 50seconds. Figure 9shows that for obtaining the disintegration time below 20 secs, the combination of concentrations of PEG and CP selected should be such that concentration of PEG should be around 15%v/w and concentration of CP in the range of 4.6%w/w to 5% w/w, concentration of HPMC being constant here i.e. 37.5%w/w. The plot also shows different areas representing the combinations of concentrations of CP and PEG and the respective disintegration times the combinations may bring about. It also indicates that any combination of concentration of CP below 4.2%w/w and PEG below 7.5%v/w, causes the disintegration time to exceed 35 seconds. Figure 10shows that the disintegration time below 15 secs, may be obtained when the combination of concentrations of PEG and HPMC selected is such that concentration of PEG is around 15% v/w and concentration of HPMC 35%w/w, concentration of CP being constant here i.e. 4.5%w/w. The plot also shows different areas representing the combinations of concentrations of HPMC and PEG and the respective disintegration times the combinations may bring about. It also indicates that any combination of 5% v/w PEG and 40%w/w HPMC, causes the disintegration time to exceed 45 seconds.The solid lines in the contour plot(figure 11) indicates the lower disintegration time i.e. 20seconds and the broken lines indicate the higher disintegration time i.e. 25 seconds, to formulate an optimized batch of fast dissolving films with the disintegration time well between 20-25 seconds, the white area between the solid and the broken lines gives various combination of concentrations of HPMC and CP, the concentration of PEG being constant i.e. 10% v/w that may be selected. Any combination of concentration within this area is capable of providing the desired lower disintegration value between 20-25 seconds. The surface plots indicate that with the increasing concentration of HPMC, the disintegration time also increases whereas with the increase in concentration of CP, the disintegration time decreases and likewise with the increase in concentration of PEG, the disintegration time decreases. The optimization of composite responses of three variables indicates that with the increase in concentration of HPMC the disintegration time increases respectively and with the increase in concentration of CP and PEG the disintegration time decreases. The plot also shows that when our target disintegration time is of 22 seconds, the combination of the three variables should be such that HPMC should be used in its lower concentrations i.e. around 35% w/w, CP should also be used in its lower concentration i.e. around 4% w/w and PEG should be used in its intermediate concentration of around 10% v/w.

Evaluation of Films: The weight of the films was determined by an analytical balance. Of all formulations, minimum weight was found to be 0.0978±0.004 mg in formulation L2 and maximum weight was found to be 0.10125±0.004 mg in formulation L9. The surface pH range was found to be between 6 and 7.74. The folding endurance was measured manually by folding the film repeatedly a point till it broke. Of all formulations, maximum folding endurance was found to be 327 in formulation L1 and minimum folding endurance was found to be 118 in formulation L3. The values indicating that as the concentration of polymer increases, the folding endurance capacity also increases, this result can be co-related with literature [1]. The thickness of films was measured using vernier cliper. Of all formulations, minimum thickness was found to be 0.243±0.073 mm in formulation L4 maximum thickness was found to be 0.369±0.033 mm in formulation L10. This finding is also in coherence with available literature which shows that as the concentration of HPMC is increased the thickness of the film increased gradually [1, 6].The content uniformity ranged from 99.66% to 101.03%. Minimum disintegration was found to be 12.33±3.326 seconds in formulation L2 and maximum disintegration was found to be 61.33±16.39 seconds in formulation L8. Though the percentage of CP used in L8 was greater than that used in L2, the concentration of HPMC use was greater in L8 than that used in L2 this may have resulted in higher DT for L8 when compared to L2. This shows a prominent effect of HPMC in disintegration time of the films and this is also in coherence with available literature which shows that DT increases with the increase in concentration of polymer [1, 6]. Figure 2 and 4 shows that batches L1, L10, with higher concentration of HPMC showed comparatively slower rates of drug release when compared to the drug release rates for batches L3 and L4 with a lower concentration of HPMC, where concentration of other variables CP and PEG remained constant. Figure 3, 5, 6 and 7 shows that batches L6, L7, L8 and L11 with higher concentrations of CP showed relatively fast drug release compared to the batches L2, L5, L9 and L13 with lower concentrations of CP with concentrations of other variables HPMC and PEG remaining constant. Minimum cumulative drug release percentage was found to be 87.687 for batch L2 and maximum cumulative drug release percentage was found to be 100.25 for batch L11.

CONCLUSIONS

From this study it can be concluded that there is a significant effect of HPMC, plasticizer PEG and Crospovidone on the characteristics and integrity of films. Increase in HPMC concentration increases the disintegration time while increasing concentration of PEG and crospovidone decreases the disintegration time of films. Hence, oral dispersible film of Levocetirizine dihydrochloride for quick relief from allergic rhinitis can be made by solvent casting method.

Acknowledgements: The authors are thankful to Lomus Pharmaceuticals Pvt. Ltd. for providing Metformin Hydrochloride and various grades of HPMC as a gift samples and National Model College for Advance Learning for providing necessary facilities to carry out this work.

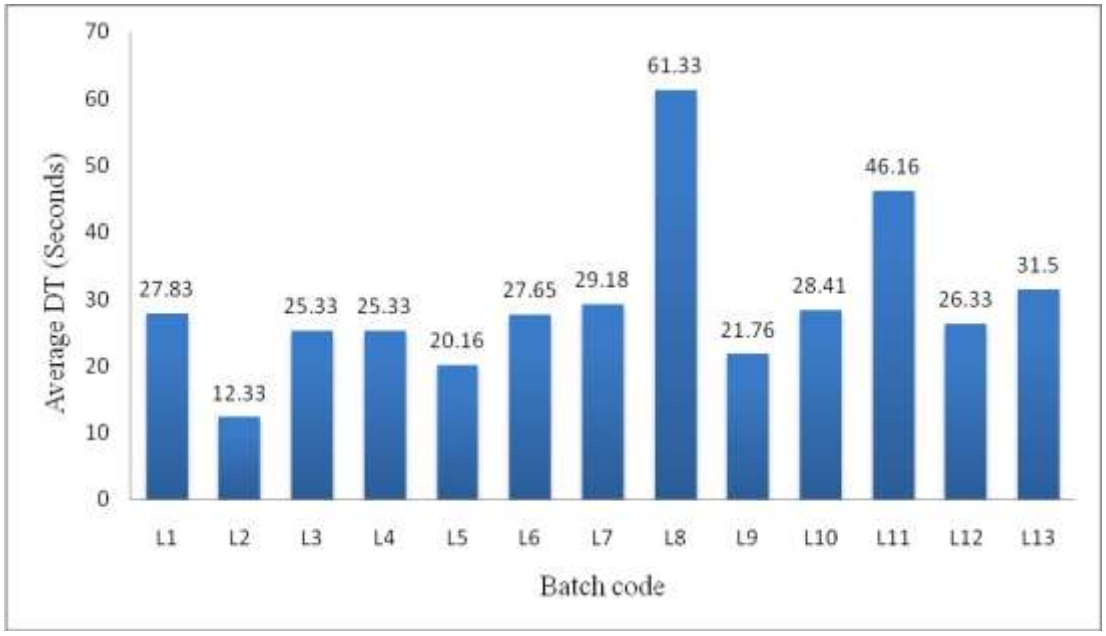

Figure 1: Bar diagram showing disintegration time of various batches of oral fast dissolving films.

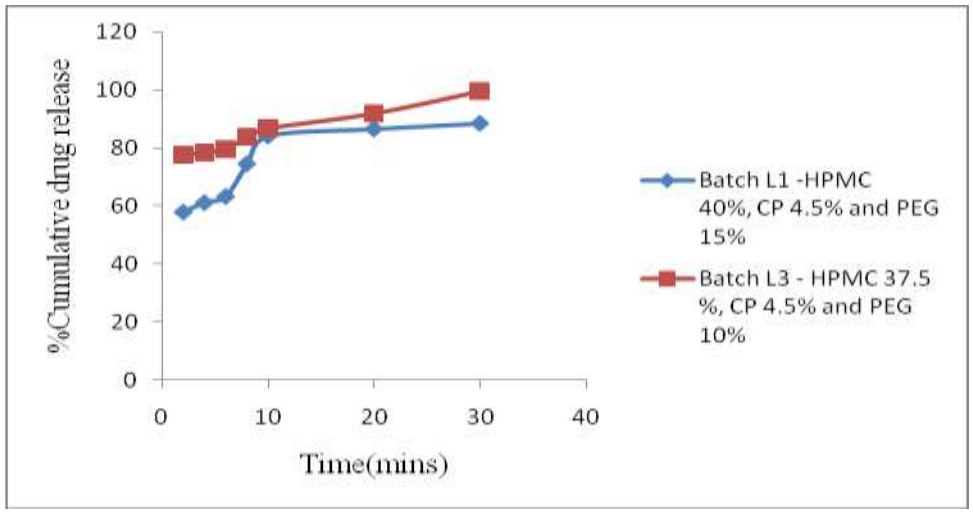

Figure 2: Effect of HPMC on cumulative percentage drug release

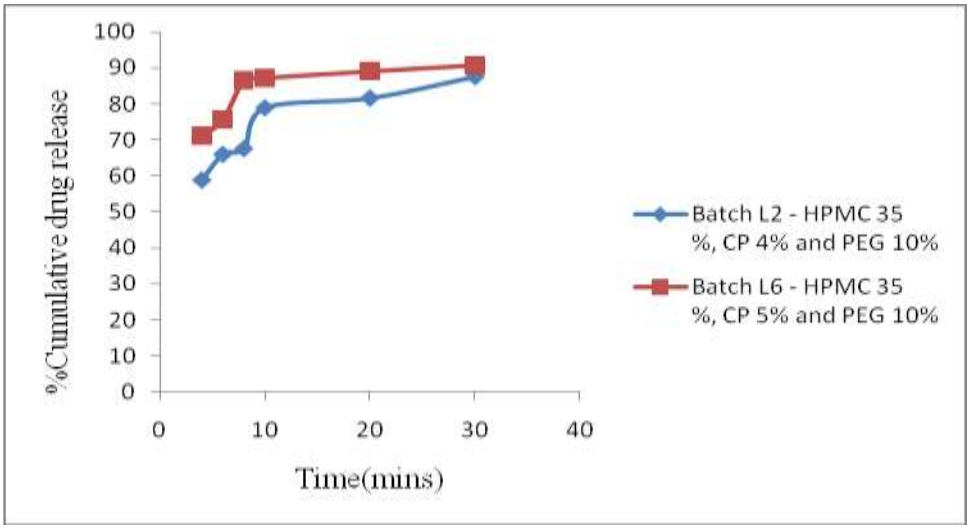

Figure 3: Effect of CP on cumulative percentage drug release

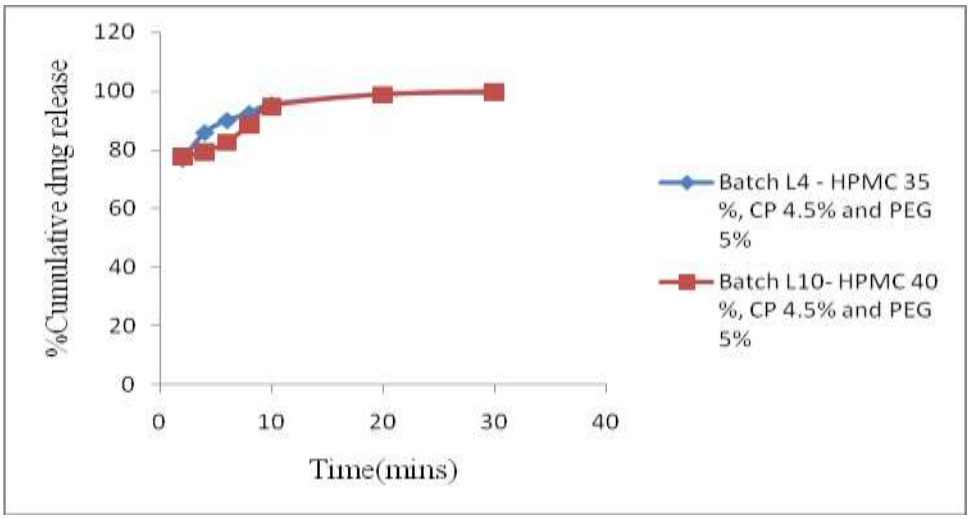

Figure 4: Effect of HPMC on cumulative percentage drug release

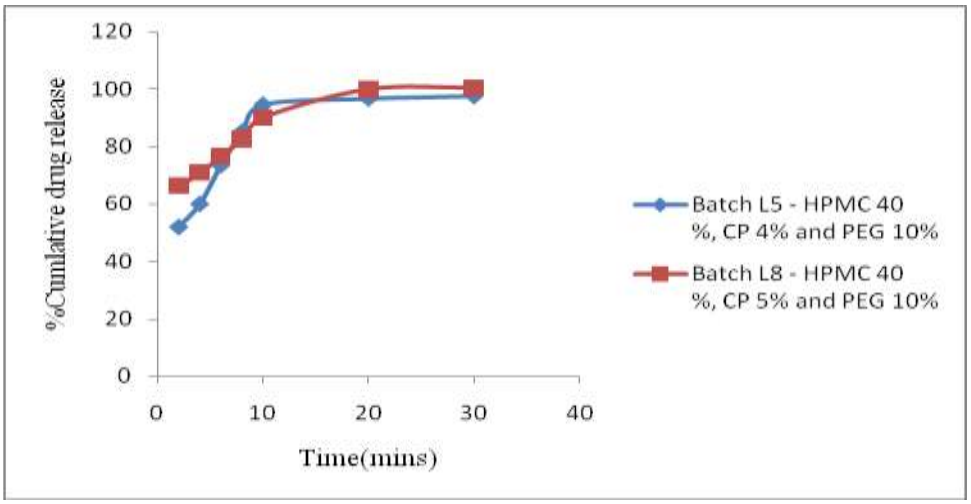

Figure 5: Effect of CP on cumulative percentage drug release

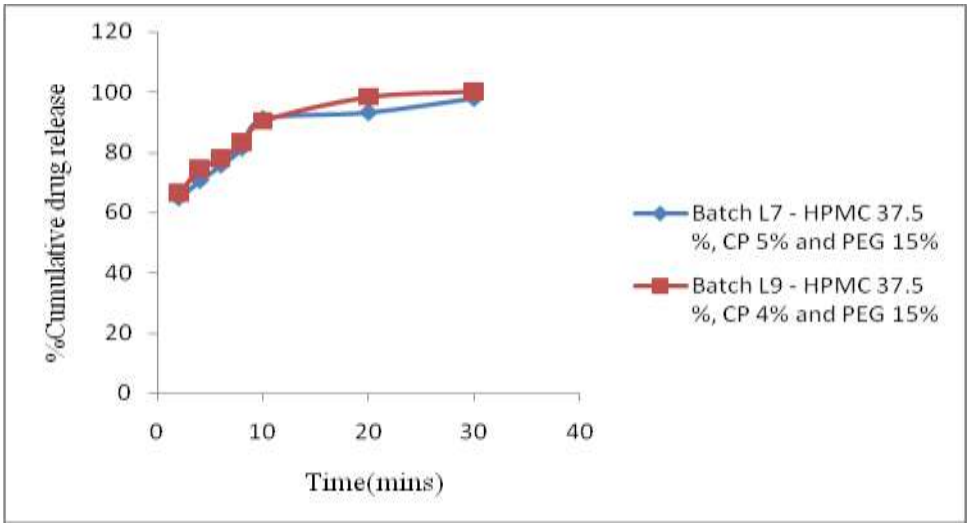

Figure 6: Effect of CP on cumulative percentage drug release

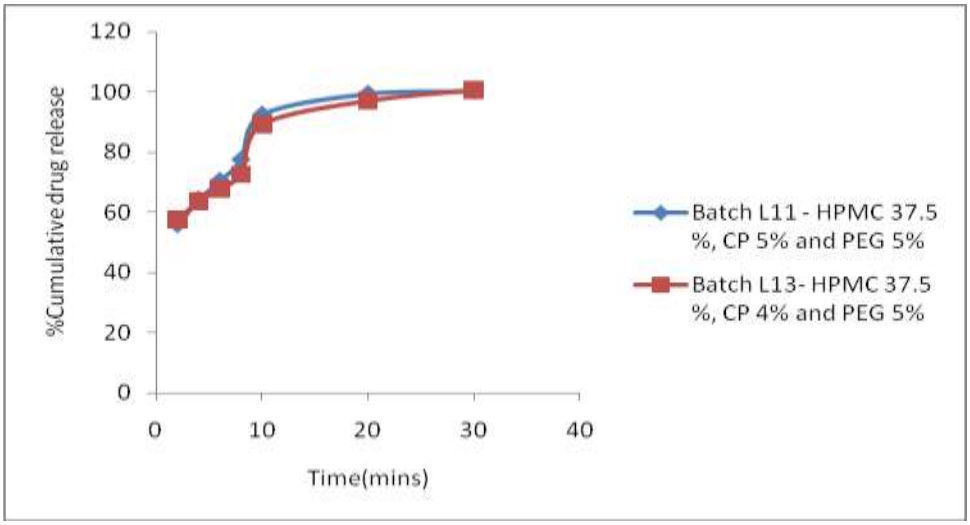

Figure 7: Effect of CP on cumulative percentage drug release

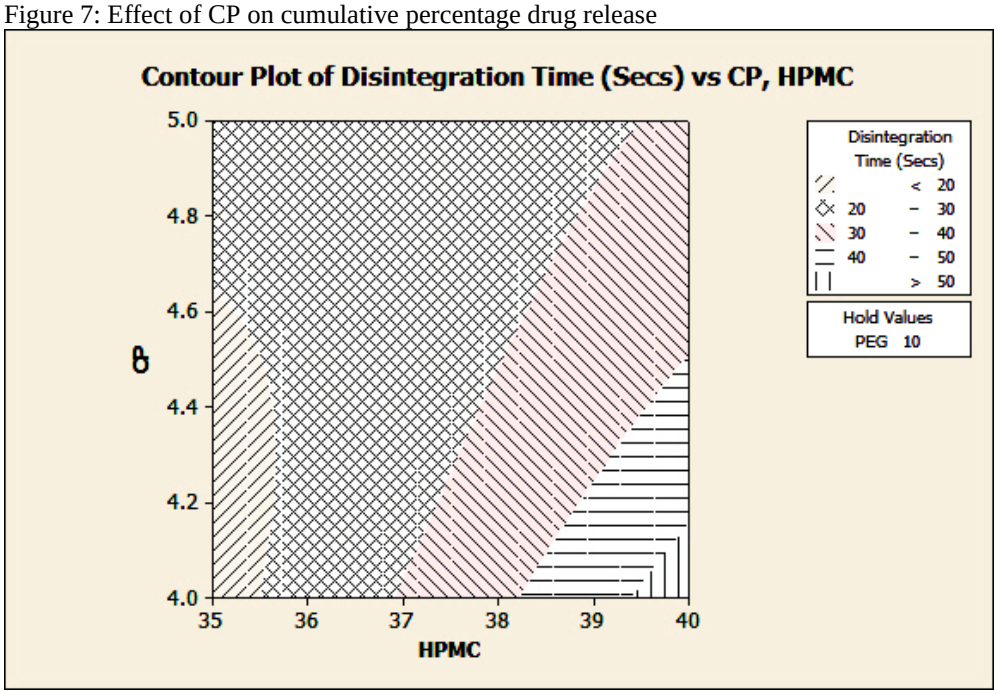

Figure 8: Contour plot of Disintegration Time (Secs) vs CP, HPMC

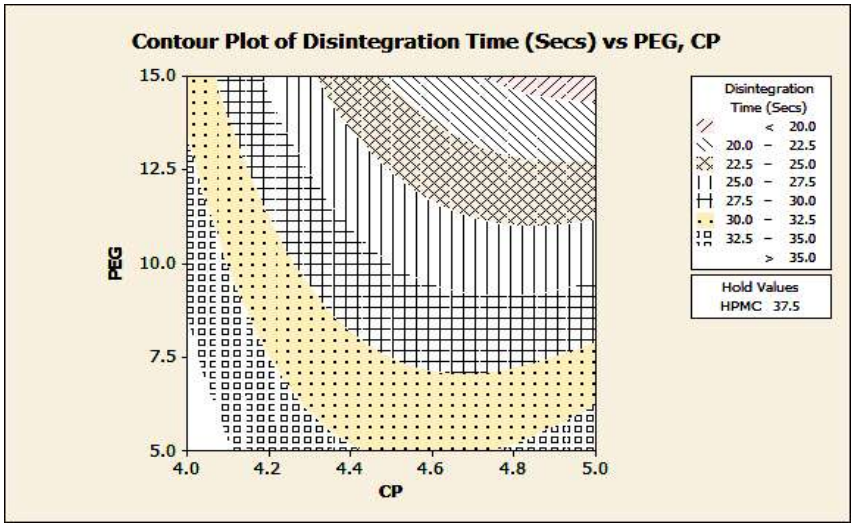

Figure 9: Contour Plot of Disintegration Time (Secs) vs PEG, CP

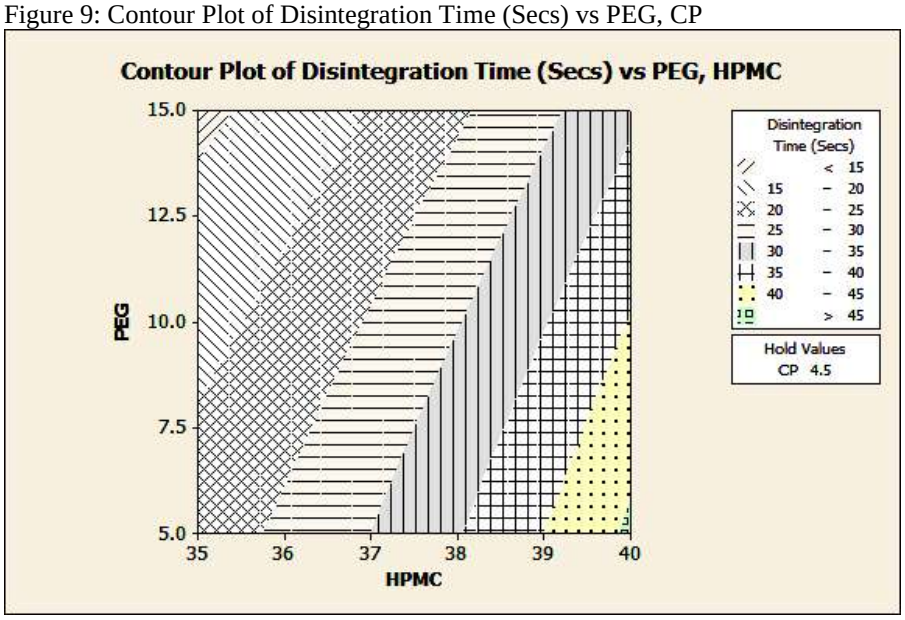

Figure 10: Contour Plot of DisintegrationTime (Secs) vs PEG, HPMC

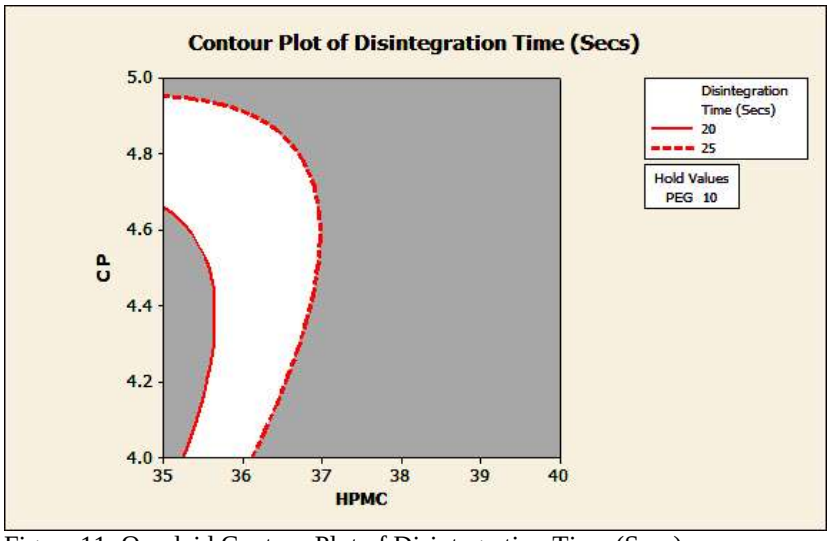

Figure 11: Overlaid Contour Plot of Disintegration Time (Secs)

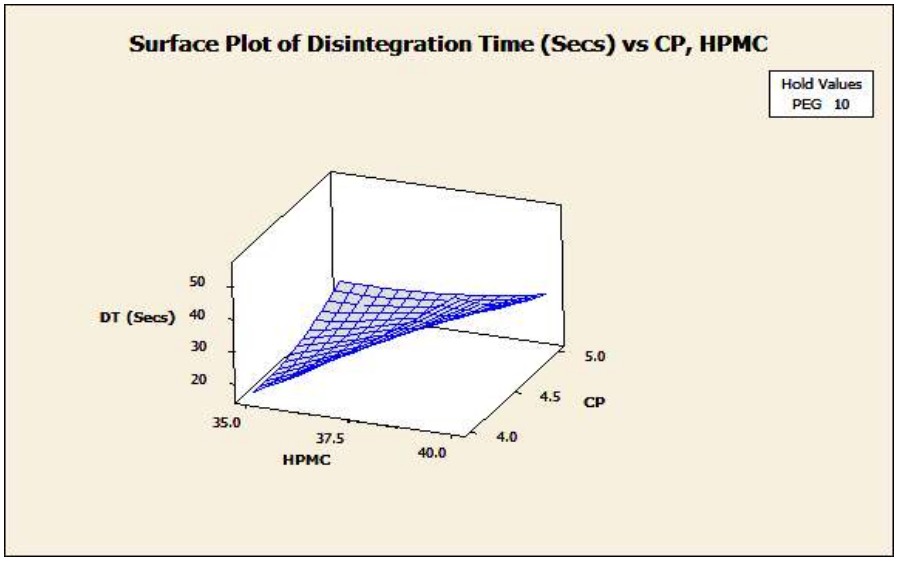

Figure 12: Surface Plot of Disintegration Time (secs) vs CP, HPMC

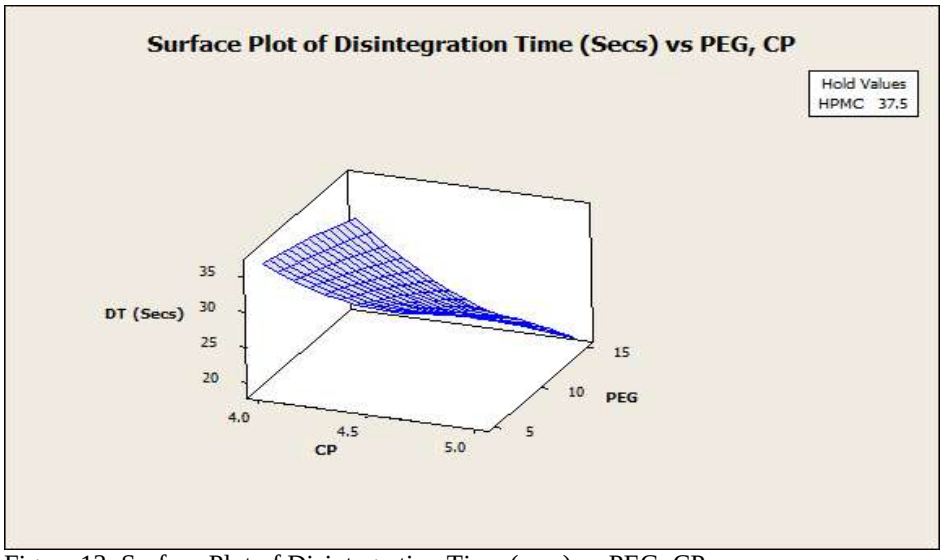

Figure 13: Surface Plot of Disintegration Time (secs) vs PEG, CP

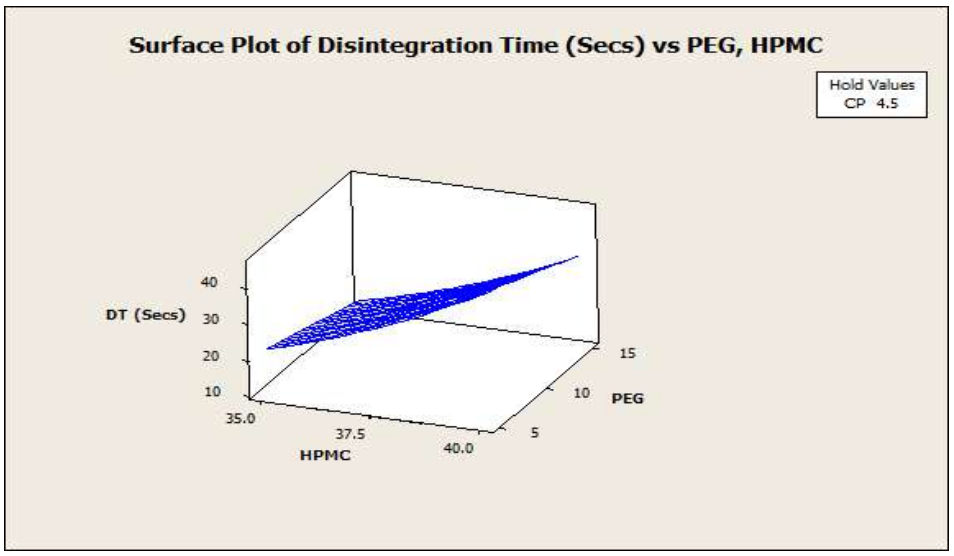

Figure 14: Surface plot of Disintegration Time (secs) vs PEG, HPMC

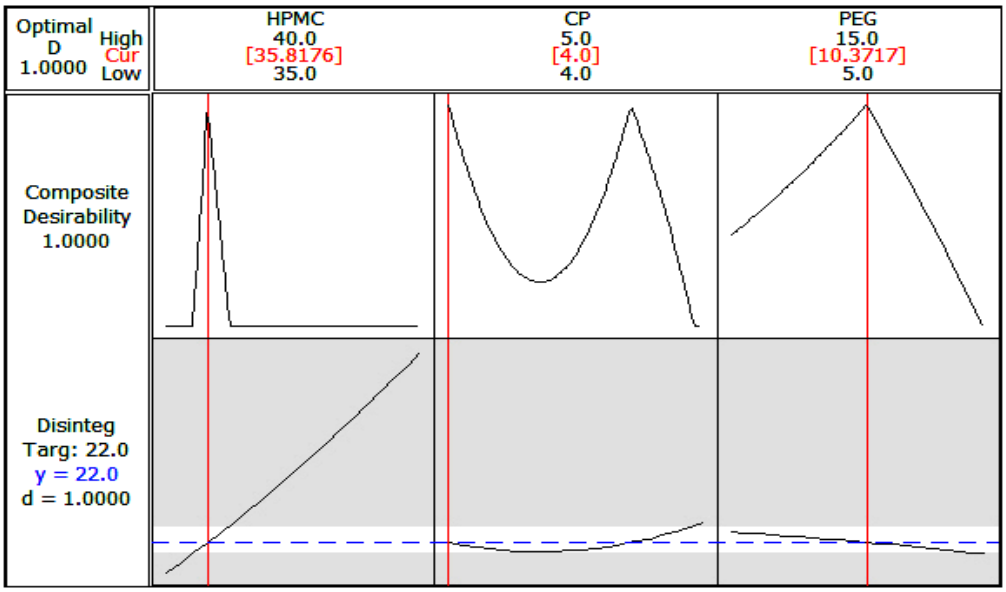

Figure 15: Optimization of composite responses of 3 variables

Table 1: Preparation of films trial batches using excipients at different concentrations

Batch code	HPMC	PEG	CCS	CP	Glycerol	DT(Sec)
P1	40%	15%	4%		15%	130
P2	40%	15%		4%	15%	30
P3	35%	20%		5%	20%	49(brittle films)
P4	45%	10%		5%	15%	130
P5	50%	12%		5%	15%	139
P6	30%	15%		4%	15%	poor film
P7	30%	15%		4%	10%	poor film
P8	35%	15%		4%	10%	39
P9	20%	18%		5%	10%	poor film
P10	22%	20%		5%	10%	poor film

Table 2: Dissolution profiles of formulated batches

Time (mins)	Batch 1- HPMC 40%, CP 4.5% and PEG 15%	Batch 2- HPMC 35.5 %, CP 4% and PEG 10%	Batch 3- HPMC 37.5 %, CP 4.5% and PEG 10%	Batch 4- HPMC 35 %, CP 4.5% and PEG 5%	Batch 5- HPMC 40 %, CP 4% and PEG 10%	Batch 6- HPMC 35 %, CP 5% and PEG 10%	Batch 7- HPMC 37.5 %, CP 5% and PEG 15%	Batch 8- HPMC 40 %, CP 5% and PEG 10%	Batch 9- HPMC 37.5 %, CP 4% and PEG 15%	Batch 10- HPMC 40 %, CP 4.5% and PEG 5%	Batch 11- HPMC 35.5 %, CP 5% and PEG 5%	Batch 12- HPMC 35 %, CP 4.5% and PEG 15%	Batch 13- HPMC 37.5 %, CP 4% and PEG 5%
2	57.96	55.21	77.77	76.87	51.975	63.161	64.81	66.32	66.32	77.81	55.82	66.48	57.45
4	61.22	58.88	78.585	85.93	59.98	71.17	70.58	70.8	74.56	79.42	64.22	72.87	63.555
6	63.34	66.03	79.64	90.07	73.41	75.7	75.71	76.7	77.9	82.76	70.45	82.48	67.82
8	74.57	67.62	83.98	92.51	85.03	86.54	81.36	82.55	83.32	88.7	77.44	91.66	72.62
10	84.18	79	86.817	95.58	94.44	87.28	91.04	90.08	90.505	94.91	92.45	96.67	89.14
20	86.61	81.69	91.945	98.93	96.55	89.12	93.16	99.83	98.415	98.81	99.355	99.45	97.04
30	88.53	87.68	100.051	99.288	97.42	90.81	97.825	100.4	100.29	99.88	100.2	100.26	100.6

Table 3: Physicochemical parameter analysis of formulations prepared by sublimation approach

Batch code	spl 1	spl 2	spl 3	spl 4	spl 5	spl 6	Mean ± SD
L1	100.4	101	101.4	102	100.2	101.2	101.033 ± 0.662
L2	100.8	100.6	99.4	100.6	100.6	100.8	100.433 ± 0.527
L3	100.2	101	98	98.4	98.4	99.8	99.666 ± 1.1211
L4	100.4	99.4	100.2	99.2	99.2	100.12	100.086 ± 0.722
L5	98.6	99.8	101.2	100.2	100.2	101.14	100.266 ± 1.017
L6	100.4	100.4	100.6	100.6	100.6	100.6	100.443 ± 0.211
L7	100.06	100.2	100.2	99.4	99.4	99.7	99.96 ± 0.335
L8	99.8	100.04	100.4	99.4	99.4	100.02	99.946 ± 0.330
L9	100.6	99.2	100.18	100.2	100.2	100.2	100.083 ± 0.456
L10	100.8	100.4	100.4	99.4	99.4	100.02	100. 173 ± 0.477
L11	99	98.8	100.2	100.8	100.8	100.4	99.933 ± 0.826
L12	101.4	101.8	100.2	101.8	101.8	101.2	101.033 ± 0.843
L13	100.8	99.6	100.4	100.8	100.8	99.8	100.1 ± 0.666

Table 4: Evaluation of oral fast dissolving films for weight variation, surface pH, folding endurance and thickness

Batch Code	Weight variation (Mean ± SD)	Surface pH	lding Endurance	Thickness (Mean ± SD)
L1	0.100±0.004	7.13	327	0.336±0.032
L2	0.097±0.004	7.68	145	0.264±0.032
L3	0.099±0.002	6.68	118	0.271±0.023
L4	0.098±0.004	7.74	130	0.243±0.073
L5	0.100±0.005	7.41	185	0.356±0.017
L6	0.100±0.003	6.21	197	0.272±0.017
L7	0.099±0.004	7.12	130	0.312±0.029
L8	0.100±0.004	7.41	186	0.341±0.025
L9	0.101±0.0044	6	171	0.273±0.0483
L10	0.100±0.003	6.08	314	0.369±0.033
L11	0.100±0.004	6.77	146	0.315±0.024
L12	0.099±0.003	6.93	125	0.252±0.026
L13	0.099±0.003	6.02	131	0.323±0.029

Table 5: Evaluation of oral fast dissolving films for content uniformity and disintegration time

Batch code	Content Uniformity (Mean ± SD)	Disintegration time (Mean ±SD)	% Cumulative drug release (Mean ± SD)
L1	101.03±0.662	27.83333±7.25	88.53 ± 5.732
L2	100.43±0.527	12.33±3.32	87.687 ± 3.3986
L3	99.66±1.210	25.33±11.70	100.051 ± 0.721
L4	100.08±0.722	25.33±11.70	99.288 ± 1.110
L5	100.26±1.017	20.16±11.990	97.423 ± 3.308
L6	100.44±0.211	27.65±8.76	90.86 ± 3.870
L7	99.96±0.33	29.18±6.26	100.29 ± 0.563
L8	99.94±0.330	61.33±16.39	100.445 ± 0.619
L9	100.0833±0.477	21.766±8.56	97.825 ± 1.356
L10	100.1733±0.477	28.416±8.569	99.885 ± 0.561
L11	99.93333±0.826	46.16±16.95	100.71 ± 0.864
L12	101.0333±0.843	26.33±9.953	100.26 ± 0.270
L13	100.1±0.666	31.50±15.10	100.25 ± 0.737

REFERENCES

1. Prasanthi, N. L., Krishna, C. S., Gupta, M. E., Manikiran, S. S., & Rao, N. R. (2011). Design and Development of Sublingual Fast Dissolving Films for an Antiasthmatic Drug. *Scholars research library*, *3*(1), 382-395.
2. Mahaparale, M. A., Shivnikar, S. S. T., Pawar, K. V., & Prashant, N. Fast dissolving oral films: an innovative drug delivery system.
3. Siddiqui, M. N., Garg, G., & Sharma, P. K. (2011). A short review on "A novel approach in oral fast dissolving drug delivery system and their patents".*Advances in Biological Research*, *5*(6), 291-303.
4. Bircan, Y., & Çomoğlu, T. (2012). Formulation technologies of orally fast disintegrating tablets. *Marmara Pharmaceutical Journal*, *16*, 77-81.
5. Jesmeen, T., & Uddin, R. (2011). Orodispersible Tablets: A Short Review.*Stamford Journal of Pharmaceutical Sciences*, *4*(1), 96-99.
6. Bhyan, B., Jangra, S., Kaur, M., & Singh, H. (2011). Orally fast dissolving films: innovations in formulation and technology. *International Journal oF Pharm Sciences and Research Res*, *9*, 9.
7. Desu, P. K., Brahmaiah, B., Nagalakshmi, A., Neelima, K., Nama, S., & Baburao, C. (2013). An overview on rapid dissolving films. *Asian Journal of Pharmaceutical Research. Vol*, *3*(1), 15-23.
8. Kalyan, S., & Bansal, M. (2012). Recent trends in the development of oral dissolving Film. *International Journal PharmTech Research*, *4*, 25-33.
9. Jadhav, S. D., Kalambe, N. R., Jadhav, C. M., Tekade, B. W., & Patil, R. V. (2012). Formulation and evaluation of fast dissolving oral film of levocetirizine dihydrochlorid. *International Journal of Pharmacy and Pharmaceutical Sciences*, *4*(1), 337-341.
10. Sreekanth, M. J., & Lakshmi, M. P. Formulation development of fast releasing oral thin films of Levocetirizine dihydrochloride with eudragit epo and optimisation through taguchi orthogonal experimental design.
11. Saini, P., Kumar, A., Sharma, P., & Visht, S. (2012). Fast Disintegrating Oral Films: A Recent Trend of Drug Delivery. *International Journal of Drug Development& Research*, *4*(4), 80-94.