International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 3, 2025
https://www.theaspd.com/ijes.php

Formulation And Evaluation Of Furosemide Mouth Dissolving Films

Mr. Babshetty Rohit Basavraj*[1], Dr.Manish Kumar[2]

[1]Research Scholar, Faculty of Pharmaceutical Sciences Madhav University,Abu Road Pindwara Sirohi Rajasthan. Email.Id.-babshettyrohit@gmail.com
[2]Professor, Faculty of Pharmaceutical Sciences Madhav University,Abu Road Pindwara Sirohi Rajasthan. Email.Id.- manishsip@gmail.com
Corresponding Author
Mr.Babshetty Rohit Basavraj, Research Scholar, Faculty of Pharmaceutical Sciences Madhav University,Abu Road Pindwara Sirohi Rajasthan. Email.Id.-babshettyrohit@gmail.com

Abstract *To improve patient convenience and drug delivery, mouth-dissolving films (MDFs) were formulated using HPMC E5 as film-forming polymer, PEG-400 as plasticizer, and croscarmellose sodium as the super disintegrant. The Box-Behnken design was utilized to optimize the concentrations of the components and evaluate their impact on disintegration time, tensile strength, thickness, folding endurance, and drug content. Stability studies of the films were performed according to ICH guidelines to establish their shelf life. The promising film 99.18 ± 3.32% (F8) showed the greatest drug dissolution (more than 75% within 15 min), satisfactory in vitro disintegration time 27 ± 1.88 seconds.*

Keywords: *Furosemide, Mouth Dissolving Films, HPMC E5*

INTRODUCTION:

Mouth-dissolving films (MDFs) are another innovative approach to enhance drug delivery. They provide rapid disintegration and drug release, bypassing the need for water, which improves patient adherence [1]. Hydroxypropyl methylcellulose (HPMC) is commonly used as a film-forming polymer in MDFs, offering favorable mechanical properties and controlled dissolution[2]. These films offer an efficient means to deliver poorly soluble drugs like Furosemide by improving their solubility and dissolution rate [3].

This study aims to develop and optimize Furosemide mouth-dissolving films to enhance drug solubility, release rate, and stability. Mouth-dissolving films were formulated using HPMC E5. The research employs a Box-Behnken design that optimizes the concentrations of film-forming polymer, plasticizer, and super-disintegrant. These efforts highlight the potential of MDFs for improving therapeutic outcomes[4].

METHOD

SELECTION OF FILM-FORMING POLYMER

Selecting the appropriate polymer is essential for the successful manufacturing of orally disintegrating films (ODFs), as this choice significantly influences the mechanical strength of the films. Polymers can be utilized individually or in combination with other polymers to modify film properties.

Another important aspect to consider when developing an ODF is the concentration of the polymers used. It is vital to carefully choose and understand the polymer to maintain the integrity of the quick-dissolving oral films. To obtain the desired properties and functionality of the film, the polymer concentration in ODF preparation usually ranges from 60% to 65% w/w of the dry film's total weight, with an average of approximately 45% w/w.Various polymers have been tested in creating mouth-dissolving films to identify the one that provides optimal characteristics[4].

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 3, 2025
https://www.theaspd.com/ijes.php

CALCULATION OF AMOUNT OF DRUG PER BATCH OF FILM (DOSE CALCULATION OF FUROSEMIDE)

Effective dose of Furosemide = 80 mg

Radius of petri dish = 4.5 centimetre

Area of Petri dish : πr^2 == 3.14 * 4.5 * 4.5 = 63.5cm^2

Area of petri dish x Amount of drug / Aa of film = 63.5 *20 /4 = 317.925

400mg of solid dispersions = 80 mg of drug

Hence, X = ????

X = 317.925 X400/80 = 1589.62 mg

Number of patches = Area of Petri dish / Area of film = 63.585/ 4 = 15.84 patches

Solid dispersion per patch = 1589.62/ 15.84 = 100mg = 0.1 gm[5]

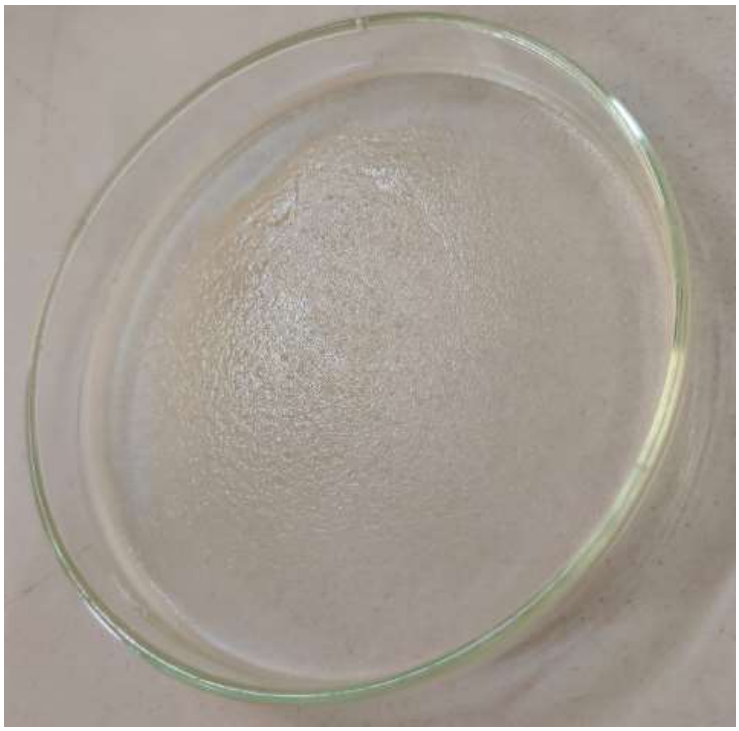

Figure 1: Photographs of Mouth-dissolving film of Optimized Batch

OPTIMIZATION OF MOUTH-DISSOLVING FILMS

Formulation was developed using Design Expert® software employing a randomized full factorial design for optimization. Three factors were assessed at three levels, generating 13 unique combinations without repetitions. This approach was used to assess the effects of independent variables on the characteristics of orally disintegrating films [6].

The three chosen independent variables were the amount of film-forming polymer (A), the level of super disintegrant (B), and the quantity of plasticizer (C).

The dependent variables assessed included disintegration time (Y1) and the percentage of drug released within 90 seconds (Y2)[6].

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 3, 2025
https://www.theaspd.com/ijes.php

Table 1 - Independent variables and levels of it using Box-Behnken design

Variation in Independent variables	Level Low (-1)	Level Medium (0)	Level High (+1)
Concentration of film-forming polymer in mg (A) [HPMC E5]	300	500	700
Concentration of super disintegrant in mg (B) [Croscarmellose sodium]	5	17.5	30
Concentration of plasticizer in ml (C) [PEG - 400]	0.1	0.3	0.5

Table 2 –Dependent variables selected for optimization study

Disintegration time	Y1	Response1
% of drug released at 90 seconds	Y2	Response 2

Table 3: Composition of mouth dissolving films

Formulation code	Concentration of polymer (mg)	Concentration of plasticizer (ml)	Concentration of super-disintegrant (mg)	Concentration of sweetener (mg)	Concentration of saliva stimulating agent (mg)
F1	400	300	150	50	5
F2	600	190	400	50	5
F3	400	190	275	50	5
F4	400	80	400	50	5
F5	600	80	275	50	5
F6	200	190	150	50	5
F7	400	190	275	50	5
F8	400	300	400	50	5
F9	400	190	275	50	5

F10	400	190	275	50	5
F11	200	80	275	50	5
F12	600	190	150	50	5
F13	200	190	400	50	5
F14	400	190	275	50	5
F15	400	80	150	50	5
F16	200	300	275	50	5
F17	600	300	275	50	5

FORMULATION OF MOUTH-DISSOLVING FILMS

The film was produced using the solvent casting technique, where the film-forming polymer HPMC E5 was initially dissolved in an adequate amount of distilled water. Meanwhile, all other excipients, along with the drug extract, including croscarmellose sodium (a super-disintegrant), polyethylene glycol (a plasticizer), and citric acid (a saliva-stimulating agent), were dissolved separately in the remaining distilled water. The polymer solution was placed on a magnetic stirrer and stirred at 300 rpm until fully dissolved.

The solution containing the excipients and drug was then added in the polymer solution and was stirred for one hour. The mixture was kept then at room temperature for an hour that eliminates any bubbles and foam formed. It was subsequently poured into a lubricated petri dish and left to dry for 24 to 48 hours. Once dried, the film was removed and carefully cut into 2 cm x 2 cm pieces[7].

EVALUATION OF ORALLY DISINTEGRATING FILMS

FILM FORMING CAPACITY

The film formed was evaluated for appearance, smoothness, texture, and color and was rated on a scale of - + (lowest) to +++++ (highest)[8].

DISINTEGRATION (DT) TIME

DT of the film was assessed by immersing it in 10 mL of distilled water and recording the time at which the film started to disintegrate. All measurements were illustrated in triplicate[8].

FOLDING ENDURANCE

Folding endurance measures the mechanical properties of a film by determining how many times it can be folded at a 180° angle at the same point before breaking. A higher folding endurance indicates better mechanical strength. This strength is influenced by the concentration of plasticizers, which also affects folding endurance. To assess flexibility, a 2 x 2 cm strip of film is folded at the same location repeatedly until it breaks. A film that endures 300 folds or more is regarded as having excellent flexibility.

All tests were conducted in triplicate[9].

THICKNESS

We need to measure the thickness because it shows how much drug is in the OTF(Oral Thin Film). At the same time, an appropriate thickness is crucial for the convenient use of the films.

Thickness of film was calculated: using a micrometer or screw gauge. All observations were performed in

triplicate.

MOUTH DISSOLUTION TIME

The mouth dissolution time was observed by placing the film in 50 ml 6.8 pH phosphate buffer in a beaker and noting the time when the film completely dissolves with occasional shaking. All readings were performed in triplicate.

TENSILE STRENGTH

The film was stretched at two ends vertically; the lower end being attached to a weight pan. Gradually, at an interval of every 15 seconds, weights were added in ascending order, and the point at which the film broke was noted down for the calculation of tensile strength. All readings were performed in triplicate[9].

$$\text{Tensile strength} = \frac{\text{force at break(N)}}{\text{thickness of film (in mm) x width of film (in mm)}}$$

WEIGHT VARIATION

Five different cross-sectional areas of the film were cut out of the same film and the films were individually weighed for calculating weight variation.

Films measuring 1x1 cm^2 were cut from each formulation, and weight variation was determined by individually weighing them on a sensitive scale[9].

PERCENT DRUG CONTENT

Film was dissolved in 10 mL of phosphate buffer (pH 6.8) in a conical flask to achieve a concentration of 15 mg/mL. A 1 mL aliquot of this solution was then diluted to 10 mL with the same buffer, resulting in a final concentration of 1.5 mg/mL. The solution was sonicated for 10 minutes, filtered, and its absorbance was measured at 206 nm. The drug content in the film was determined using a calibration curve. All measurements were illustrated in triplicate [10].

%Drug Content→

(Practical amount of solid dispersion/Theoretical amount of solid dispersion) *100

PERCENT DRUG RELEASE AT 90 SECONDS

The film was placed in a basket apparatus with 500 mL of phosphate buffer at pH 6.8, maintained at 37 ± 0.5°C. The apparatus was operated at 50 rpm. Every 15 minutes, 5 mL of solution was withdrawn, filtered, and the absorbance was measured at 206 nm. The drug concentration in the solution was calculated using a calibration curve. All measurements were taken in triplicate [10].

Mechanism of Drug Release

To evaluate the in vitro drug release data, the release profiles were analyzed using different mathematical models. The models considered include the zero-order rate model (Eq. 1), which assumes a constant drug release rate independent of concentration; the first-order model (Eq. 2), which indicates a concentration-dependent release rate; Higuchi's model (1963) (Eq. 3), which describes drug release from an insoluble matrix as a time-dependent process following Fiskian diffusion; and the Korsmeyer et al. (1983) model (Eq. 4), which characterizes drug release from polymeric systems [11].

The following equations were used to describe the drug release models:

Eq.(1): $C = K_0 * t$

Here, K_0 : zero-order rate constant (unit = conc/time), & t represents time.

Eq.(2): $\text{Log } C = (\text{Log}C_0 - Kt) / 2.303$

Here, C_0 : initial drug-concentration & K = first-order rate constant.

Eq.(3): $Q = K^* t^{(1/2)}$

K : constant that reflects = design variables present in the system.

Eq.(4): $Mt./M\infty = K^* t^n$

Mt./ M∞ : fraction of the drug released in time t, K = rate constant, and n = release exponent.

Based on these equations, plots were constructed for each model to illustrate **mechanism of how much drug is released [11].**

STABILITY STUDIES

Following the International Council for Harmonisation i.e. (ICH) guidelines, the stability of orally dissolving films (OTFs) is evaluated under controlled environmental conditions (25°C/60% : relative humidity & 40°C/75%: relative humidity) that to for one year. During storage, OTFs are monitored for weight uniformity, morphological properties, film thickness, tensile strength, water content, and dissolution at specified time intervals. Stability testing of mouth-dissolving films follows the ICH stability guidelines outlined in Q1A (R2). The objective of these studies is to assess the shelf life of the dosage form and ensure that the drug product remains within the specified limits over time [12].

PHYSICOCHEMICAL PARAMETERS OF MOUTH-DISSOLVING FILMS

Film-Forming Capacity: The formulations exhibited varied film-forming capacities. Most formulations showed strong film-forming properties, denoted by "+++," with a few showing moderate ("++") or weak ("+") capacities. F3, F5, F9, and F11 showed weaker capacities compared to others [13].

Disintegration Time: The disintegration time ranged from 27 ± 1.88 seconds (F8) to 54 ± 1.34 seconds (F6). F8 disintegrated the fastest, while F6 required the longest time. Most formulations had disintegration times within the range of 27 to 54 seconds [14].

pH: The pH values across the formulations remained consistent, ranging from 6.8 to 7.1, indicating neutral pH levels suitable for application [15].

Folding Endurance: Folding endurance varied widely among the formulations. F6 and F13 had the highest folding endurance values (92.3 ± 1 and 92.6 ± 4, respectively), while F1 and F11 had the lowest (26.33 ± 2 and 24.3 ± 2, respectively) [16].

Thickness: The thickness of the formulations was relatively uniform, ranging from 0.10 ± 0.01 mm to 0.12 ± 0.01 mm. F5 and F12 were slightly thicker at 0.12 ± 0.01 mm[17].

Mouth Dissolution Time: Mouth dissolution times ranged between 2.8 ± 1.68 minutes (F3) and 3.8 ± 1.94 minutes (F11). Most formulations dissolved within 3 to 3.6 minutes[18].

Tensile Strength: The tensile strength values ranged from 0.38 ± 0.01 MPa (F3) to 0.48 ± 0.02 MPa (F5 and F8), reflecting moderate to strong mechanical integrity[19].

Weight Variation: The weight of the formulations ranged from 250 ± 0.43 mg (F3) to 268 ± 1.07 mg (F11). Most formulations were around 254 to 263 mg[20].

Content Uniformity: Content uniformity across formulations was excellent, ranging from 96.77 ± 0.05% (F1) to 99.61 ± 0.06% (F5 and F8). This indicates consistent drug distribution[21].

Drug Release Percentage: The drug release percentage was high for all formulations, ranging from 91.995 ± 3.44% (F4) to 99.18 ± 3.32% (F8). Most formulations exhibited a drug release of over 94%[22].

± Mean value with standard deviation of three replications are considered.

OBSERVATIONS

DISINTEGRATION TIME (DT)

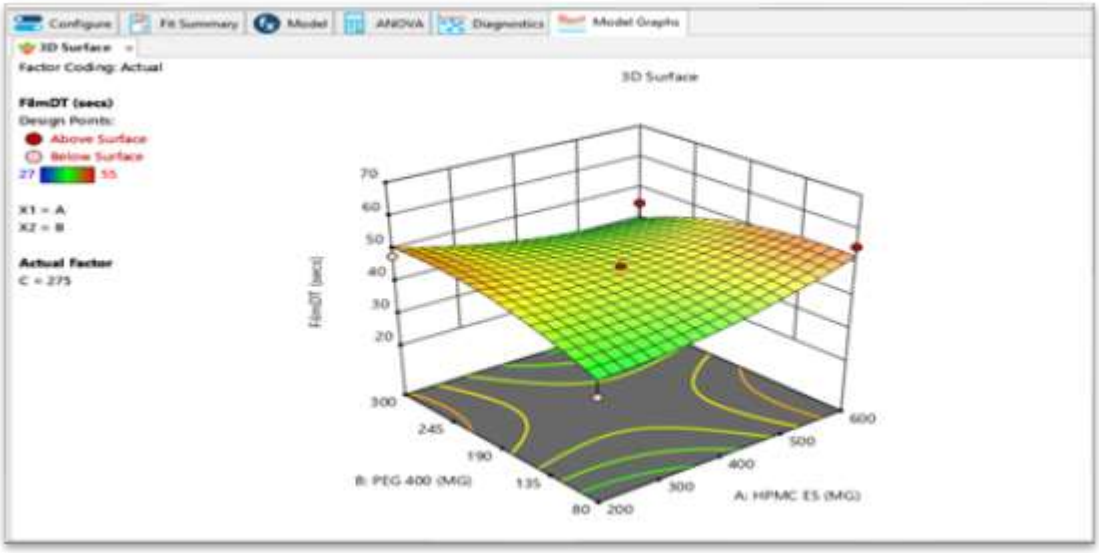

Figure 2: 3D response- surface plots for the illustration of various like Factors A i.e Polymer &B i.e Plasticizer on Disintegration time [23]

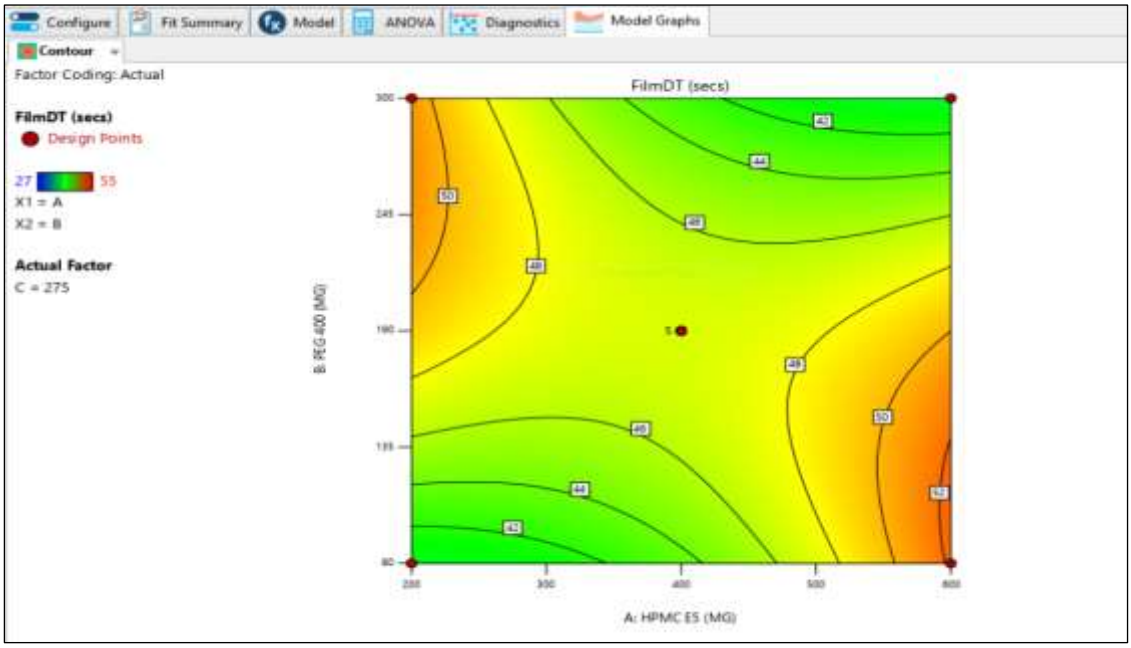

Figure 3: Contour-plot graph for illustrating , Factors A i.e Polymer & B i.e Plasticizer on DT [23]

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 3, 2025
https://www.theaspd.com/ijes.php

Response 1: FilmDT

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	671.01	9	74.56	3.87	0.0440	significant
A-HPMC E5	1.13	1	1.13	0.0584	0.8159	
B-PEG 400	1.13	1	1.13	0.0584	0.8159	
C-CROSS CARMILOSE SODIUM	24.50	1	24.50	1.27	0.2964	
AB	132.25	1	132.25	6.87	0.0344	
AC	1.0000	1	1.0000	0.0519	0.8262	
BC	25.00	1	25.00	1.30	0.2919	
A^2	29.01	1	29.01	1.51	0.2592	
B^2	63.22	1	63.22	3.28	0.1128	
C^2	390.07	1	390.07	20.26	0.0028	
Residual	134.75	7	19.25			
Lack of Fit	134.75	3	44.92			
Pure Error	0.0000	4	0.0000			
Cor Total	805.76	16				

Table 4: ANOVA table for disintegration time [24]

The Model-F.value of 3.87 shows the model is significant, with a 4.4% chance of random variation. Terms with p-values below 0.0500 (e.g., A B & C^2) are significant. Removing insignificant terms may improve model performance.

Drug release

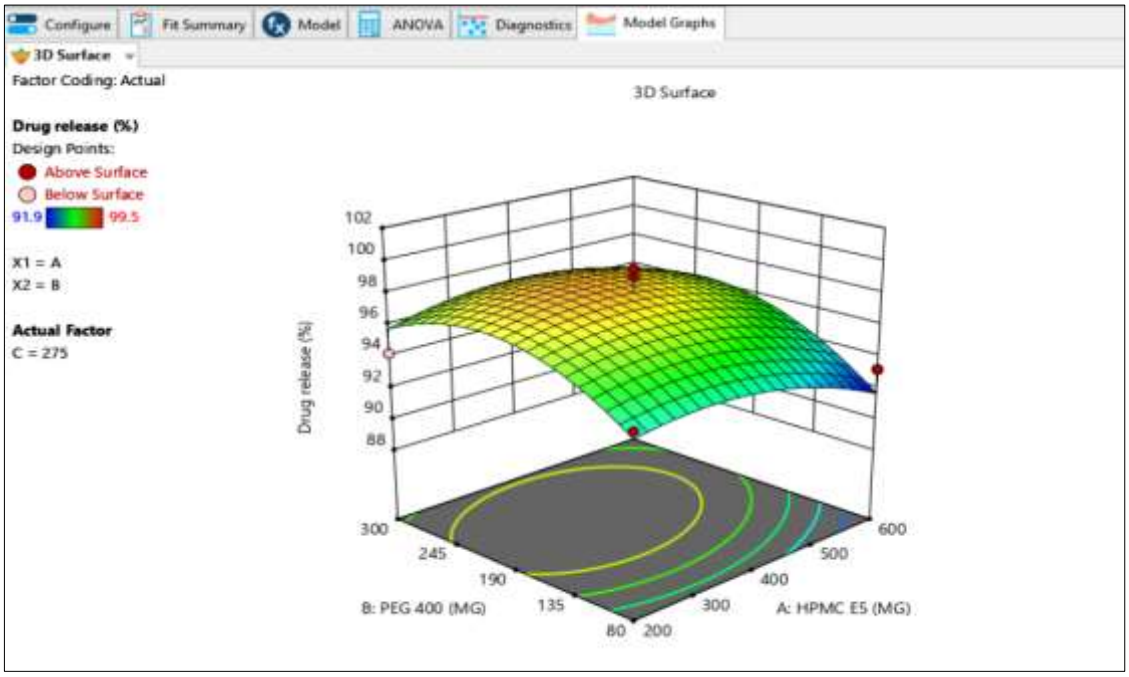

Figure 4 - 3D response-surface plots for the illustrating, Factors A i.e Polymer &B i.e Plasticizer on Drug release [25]

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 3, 2025
https://www.theaspd.com/ijes.php

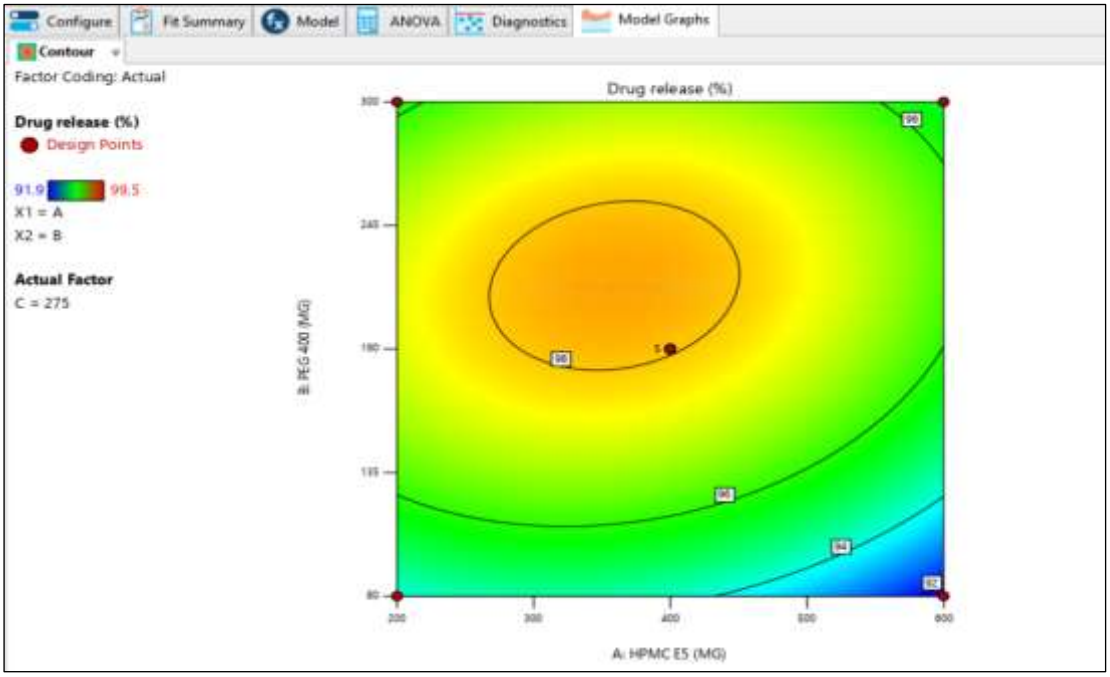

Figure 5: Contour-plot graph for the illustrating, Factors A i.e Polymer &B i.e Plasticizer on Drug release[25]

Response 2: Drug release

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	88.11	9	9.79	3.80	0.0461	significant
A-HPMC E5	3.80	1	3.80	1.47	0.2642	
B-PEG 400	14.80	1	14.80	5.74	0.0477	
C-CROSS CARMILOSE SODIUM	16.27	1	16.27	6.32	0.0402	
AB	1.01	1	1.01	0.3920	0.5511	
AC	2.34	1	2.34	0.9086	0.3722	
BC	5.74	1	5.74	2.23	0.1793	
A^2	7.85	1	7.85	3.05	0.1244	
B^2	25.23	1	25.23	9.79	0.0166	
C^2	6.96	1	6.96	2.70	0.1443	
Residual	18.04	7	2.58			
Lack of Fit	10.66	3	3.55	1.93	0.2668	not significant
Pure Error	7.37	4	1.84			
Cor Total	106.14	16				

Table 5: ANOVA table for drug release [26]

The Model-F.value of 3.80 indicates the model is significant, with a 4.61% chance of random variation. Terms with p-values below 0.0500 (e.g., C, B & B^2) are significant, while those above 0.1000 are insignificant. Simplifying the model by removing insignificant terms (except those necessary for hierarchy) may improve performance.

FOLDING ENDURANCE

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 3, 2025
https://www.theaspd.com/ijes.php

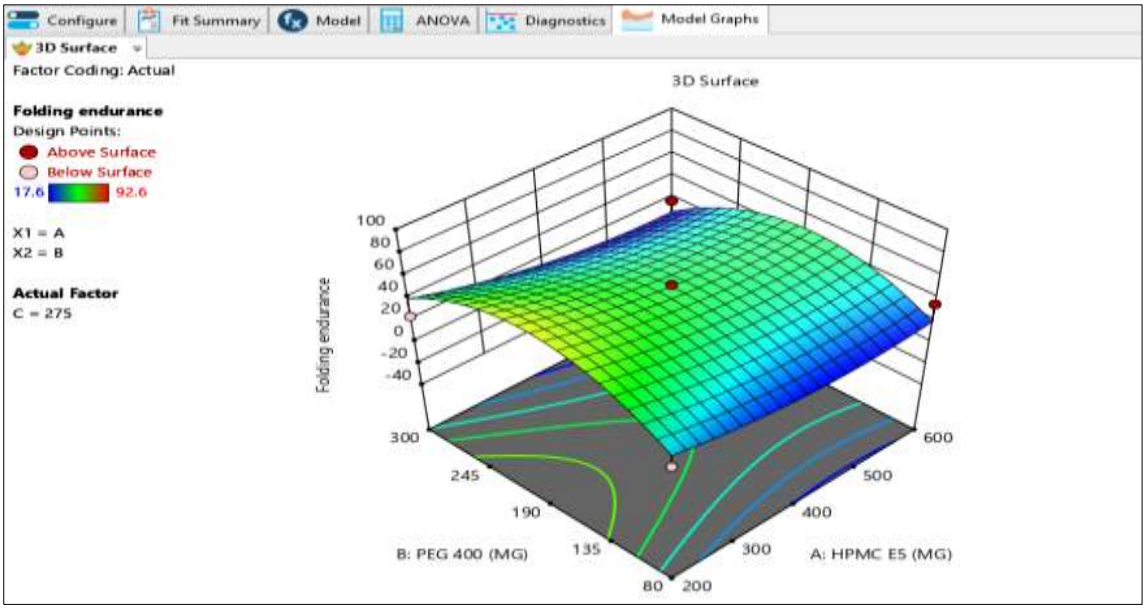

Figure 6: 3D response- surface plots for the illustrating, Factors A i.e Polymer &B i.e Plasticizer on Folding endurance [27]

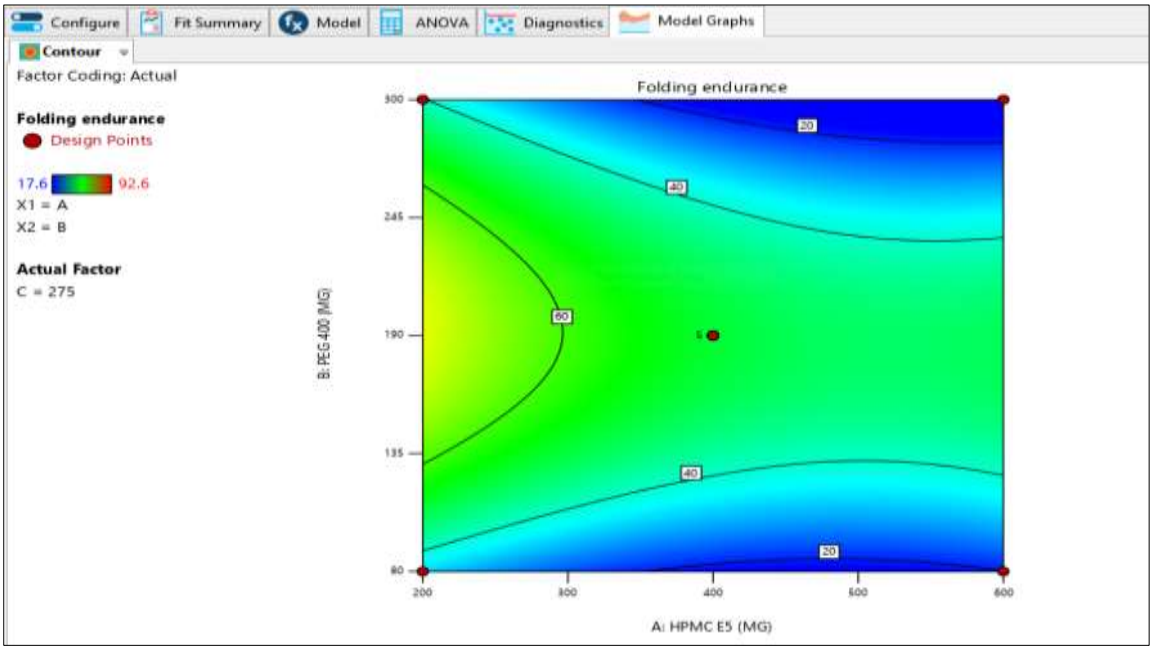

Figure 7: Contour-plot graph for the illustrating , Factors A i.e Polymer &B i.e Plasticizer on Folding endurance [27]

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 3, 2025
https://www.theaspd.com/ijes.php

Response 3: Folding endurance

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	6898.54	9	766.50	3.70	0.0491	significant
A-HPMC E5	1111.56	1	1111.56	5.37	0.0536	
B-PEG 400	17.11	1	17.11	0.0827	0.7820	
C-CROSS CARMILOSE SODIUM	80.64	1	80.64	0.3897	0.5523	
AB	90.25	1	90.25	0.4361	0.5302	
AC	54.02	1	54.02	0.2610	0.6251	
BC	5.52	1	5.52	0.0267	0.8749	
A^2	335.17	1	335.17	1.62	0.2438	
B^2	5180.91	1	5180.91	25.03	0.0016	
C^2	227.28	1	227.28	1.10	0.3295	
Residual	1448.76	7	206.97			
Lack of Fit	1423.97	3	474.66	76.59	0.0005	significant
Pure Error	24.79	4	6.20			
Cor Total	8347.30	16				

Table 5: ANOVA table for folding endurance [28]

The Model-F.value of 3.70 shows the model is statistically significant, with a 4.91% chance of random variation. Terms with p-values below 0.0500 are significant, with B^2 identified as significant. P-values above 0.1000 indicate non-significant terms. Simplifying the model by removing non-significant terms (except those needed for hierarchy) may improve performance. The Lack of Fit F-value of 76.59 indicates a significant Lack of Fit, with only a 0.05% chance of random variation. A significant Lack of Fit is undesirable, as it suggests poor model fit.

RESULTS

Regression coefficients (r) for drug release→ data from different kinetic models.

Optimized batch	Zero—order	First— order	Higuchi	Korsemeyer-Peppas	Hixson Crowell
F8	0.9054	0.9267	0.9907	0.9838	0.9767

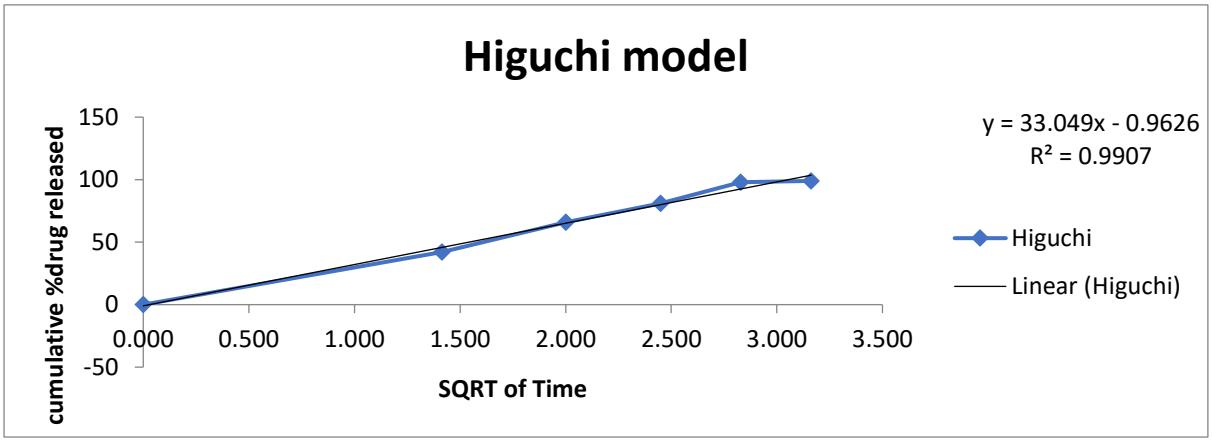

Figure 8: Higuchi model drug release kinetics for stability study of optimized batch, F8[29,30]

Table 6: Data of Optimized Formulation (F8)

Time months	Disintegration time (secs)	Folding endurance	Drug release (%)
40±2/75±5			
0	27±19	26.66±1.45	99.18±3.32
15	25±10	25.57±1.45	98.24±1.70
30	25±17	25.7±1.27	97.53±1.04

± Mean value with a standard deviation of three replicates of **optimized formulation (F8) [31].**

The stability study of the optimized batch (F8) demonstrated consistent performance over time.

CONCLUSION:

In conclusion, the mouth-dissolving films of Furosemide using HPMC E5 as polymer and croscarmellose sodium as super disintegrant showed excellent film-forming capacity, fast disintegration time (as low as 4 seconds), and high drug content uniformity (close to 99%). These films also displayed appropriate tensile strength and folding endurance, ensuring their mechanical integrity and suitability for oral disintegration. The formulations exhibited consistent drug release characteristics with rapid dissolution within 90 seconds, highlighting their potential for effective and fast-acting oral dosage forms. Overall, the oral films demonstrated significant improvements in solubility, drug release, and physical properties, supporting their use to enhance the bioavailability of Furosemide.

REFERENCES

[1] Dixit, R. P., & Puthli, S. P. (2009). Oral strip technology: Overview and future potential. Journal of Controlled Release, 139(2), 94–107.
[2] Cilurzo, F., Cupone, I. E., Minghetti, P., Selmin, F., & Montanari, L. (2008). Fast dissolving films made of maltodextrins. European Journal of Pharmaceutics and Biopharmaceutics, 70(3), 895–900.
[3] Reddy, L. H., Ghosh, B., & Rajneesh. (2002). Fast dissolving drug delivery systems: A review of the literature. Indian Journal of Pharmaceutical Sciences, 64(4), 331–336.
[4] Pawar, H., & Domb, A. J. (2018). Development and evaluation of fast dissolving films of Furosemide for enhanced bioavailability. Journal of Drug Delivery Science and Technology, 47, 310–318.
[5] Ghosh, T., Ghosh, A., & Prasad, D. (2012). A review on new generation orodispersible films and its novel evaluation techniques. Asian Journal of Pharmaceutical and Clinical Research, 5(4), 1–5.
[6] Montgomery, D. C. (2017). Design and Analysis of Experiments (9th ed.). John Wiley & Sons.
[7] Arya, A., Chandra, A., Sharma, V., & Pathak, K. (2010). Fast dissolving oral films: An innovative drug delivery system and dosage form. International Journal of ChemTech Research, 2(1), 576–583.
[8] Sogi, S. H., Hiremath, S. P., & Venkatesh, D. P. (2012). Formulation and evaluation of fast dissolving films of an antipsychotic drug. Indian Journal of Pharmaceutical Education and Research, 46(2), 118–123.
[9] Kunte, S., & Tandale, P. (2010). Fast dissolving strips: A novel approach for the delivery of verapamil. Journal of Pharmacy and Bioallied Sciences, 2(4), 325–328.
[10] Dey, P., & Maiti, S. (2010). Orodispersible tablets: A new trend in drug delivery. Journal of Natural Science, Biology and Medicine, 1(1), 2–5.
[11] Costa, P., & Sousa Lobo, J. M. (2001). Modeling and comparison of dissolution profiles. European Journal of Pharmaceutical Sciences, 13(2), 123–133.
[12] ICH Q1A (R2). (2003). Stability Testing of New Drug Substances and Products. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.
[13] Desai, P. M., Liew, C. V., & Heng, P. W. S. (2012). Review: Oral disintegrating films: Developments, technologies, and clinical applications. Drug Development and Industrial Pharmacy, 38(6), 653–664.
[14] Bhyan, B., Jangra, S., Kaur, M., & Singh, H. (2011). Orally fast dissolving films: Innovations in formulation and technology. International Journal of Pharmaceutical Sciences Review and Research, 9(2), 50–57.

[15] Cilurzo, F., Cupone, I. E., Minghetti, P., Selmin, F., & Montanari, L. (2008). Fast dissolving films made of maltodextrins. European Journal of Pharmaceutics and Biopharmaceutics, 70(3), 895–900.
[16] Nafee, N. A., Boraie, N. A., Ismail, F. A., & Mortada, L. M. (2003). Design and characterization of mucoadhesive buccal patches containing cetylpyridinium chloride. Acta Pharmaceutica, 53(3), 199–212.
[17] Dixit, R. P., & Puthli, S. P. (2009). Oral strip technology: Overview and future potential. Journal of Controlled Release, 139(2), 94–107.
[18] Preis, M., Pein, M., & Breitkreutz, J. (2012). Development of a taste-masked orodispersible film containing dimenhydrinate. Pharmaceutical Development and Technology, 17(5), 514–522.
[19] Siddiqui, 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.
[20] Yu, J., Wang, X., & Yu, Y. (2007). Development of fast dissolving oral thin films containing piroxicam. International Journal of PharmTech Research, 3(1), 279–287.
[21] Liang, A. C., & Chen, L. I. (2001). Fast-dissolving intraoral drug delivery systems. Expert Opinion on Therapeutic Patents, 11(6), 981–986.
[22] Palem, C. R., Gannu, R., Yamsani, M. R., & Rao, Y. M. (2009). Design and evaluation of bilayered mucoadhesive buccal patches of felodipine. Current Drug Delivery, 6(3), 297–305.
[23] Montgomery, D. C. (2017). Design and Analysis of Experiments (9th ed.). Wiley.
[24] Institute of Clinical Research. (2011). Design Expert Software User Guide. Stat-Ease Inc.
[25] Chaudhari, P. D., Chaudhari, S. P., Kolhe, S. R., Dave, K. V., & More, D. M. (2005). Formulation and evaluation of fast dissolving tablets of famotidine. Indian Drugs, 42(10), 641–649.
[26] Bolton, S., & Bon, C. (2009). Pharmaceutical Statistics: Practical and Clinical Applications (5th ed.). Informa Healthcare.
[27] Rowe, R. C., Sheskey, P. J., & Quinn, M. E. (2009). Handbook of Pharmaceutical Excipients (6th ed.). Pharmaceutical Press.
[28] Mahajan, A., Chhabra, N., & Aggarwal, G. (2011). Formulation and characterization of fast dissolving buccal films: A review. Scholars Research Library Der Pharmacia Lettre, 3(1), 152–165.
[29] Higuchi, T. (1963). Mechanism of sustained-action medication. Journal of Pharmaceutical Sciences, 52(12), 1145–1149.
[30] Korsmeyer, R. W., Gurny, R., Doelker, E., Buri, P., & Peppas, N. A. (1983). Mechanisms of solute release from porous hydrophilic polymers. International Journal of Pharmaceutics, 15(1), 25–35.
[31] ICH Harmonised Tripartite Guideline. (2003). Stability Testing of New Drug Substances and Products Q1A(R2). International Conference on Harmonisation.