Frontiers in Health Informatics
ISSN-Online: 2676-7104
www.healthinformaticsjournal.com
2024; Vol-13: Issue 8
Open Access

Design, Evaluation Optimization Of Oro Dispersible Film Of Felodipine Using Response Surface Method: In Vitro Characterization

Katarnavare Ambadas Bajirao[1], Dr. M. Siddaiah[2]

1. Ph.D. Scholar (Research Scholar), Department of Pharmaceutical Sciences, Bhagwant University, Rajasthan, India.
2. Research Supervisor (Honorary), Bhagwant University, Rajasthan, India.

Corresponding Author

Katarnavare Ambadas Bajirao, Ph.D. Scholar (Research Scholar), Department of Pharmaceutical Sciences, Bhagwant University, Rajasthan, India.

Email Id: ambadasbk2911@gmail.com

Cite this paper as: Katarnavare Ambadas Bajirao, Dr. M. Siddaiah (2024). Design, Evaluation Optimization Of Oro Dispersible Film Of Felodipine Using Response Surface Method: In Vitro Characterization. Frontiers in Health Informatics, Vol. 13, No.8, 7274-7288

ABSTRACT

The present study aimed to formulate and evaluate Felodipine orodispersible films (ODFs) to enhance patient compliance and provide rapid onset of action. Orodispersible films were prepared using the solvent casting method with HPMC E15 as the film-forming polymer, SSG as a superdisintegrant, PEG 400 as a plasticizer, and aspartame as a sweetener. Drug-excipient compatibility was assessed by FTIR and DSC studies. Films were evaluated for physical appearance, weight uniformity, thickness, folding endurance, tensile strength, moisture absorption/loss, drug content, in vitro disintegration, and dissolution. In vitro drug release kinetics were analyzed using zero-order, first-order, Higuchi, and Korsmeyer–Peppa's models. Stability studies were conducted under accelerated and room temperature conditions for 90 days. FTIR studies confirmed no significant interactions between Felodipine and excipients. All films demonstrated acceptable mechanical properties, rapid disintegration (F15: 11 sec), and uniform drug content (69.69–83.15%). The optimized formulation (F15) exhibited 80.10% drug release within 30 min, following a diffusion-controlled mechanism. Stability studies indicated no significant changes in physical or chemical properties over 90 days. Felodipine orodispersible films, particularly F15, were successfully developed with rapid disintegration, satisfactory mechanical strength, uniform drug content, and favourable drug release, making them a promising dosage form for improved oral delivery and patient compliance.

Keywords: Felodipine, Polymers, FTIR Studies, Solvent evaporation method, In vitro drug release studies

1.INTRODUCTION

Orodispersible films (ODFs) are thin, flexible dosage forms that rapidly dissolve or disintegrate in the oral cavity without the need for water. They are particularly advantageous for pediatric, geriatric, and dysphagic patients, improving compliance and onset of action. ODFs are typically composed of hydrophilic polymers, plasticizers, sweeteners, flavors, and active pharmaceutical ingredients (APIs). Upon placement on the tongue or buccal mucosa, the film

absorbs saliva, rapidly hydrates, and releases the incorporated drug for local or systemic absorption.[1] The small size, thinness, and flexibility of ODFs enhance patient compliance, portability, and ease of administration. The development of ODFs involves careful selection of polymers, plasticizers, and excipients to optimize mechanical strength, flexibility, disintegration time, and drug release profile. Modern formulation approaches often employ design of experiments (DoE) and response surface methodology to systematically optimize these parameters for maximum therapeutic efficacy and patient acceptability.[2] Felodipine, a calcium channel blocker, is widely prescribed for hypertension and angina. Oral administration of conventional tablets may be associated with poor patient compliance due to swallowing difficulties, especially in geriatric and pediatric populations.[3] Orodispersible films (ODFs) provide an innovative alternative, offering rapid disintegration in the oral cavity without the need for water, improving patient compliance and potentially enhancing bioavailability. ODFs are thin, flexible films that dissolve or disintegrate in the mouth, releasing the drug for local or systemic absorption. Response Surface Methodology (RSM) is a statistical tool that allows optimization of multiple formulation variables simultaneously, providing insights into their effects on critical quality attributes of the final product.[4] The present study utilizes RSM to optimize the concentration of HPMC E15 and sodium starch glycolate to achieve the ideal combination for Felodipine ODFs.

2.MATERIALS AND METHODS

Felodipine was collected as a gift sample from Hetero Labs, Hyderabad and various excipients like polymers and other excipients were purchased from Synpharma Research Labs, Hyderabad.

2.2 METHODOLOGY

Drug-Excipient Compatibility Study by FTIR[5]

In the formulation of Felodipine Oro dispersible film formation, API and Excipient may interact as they are in close communication with each other, which could lead to the instability of drug.

FT-IR spectroscopy was employed to ascertain the compatibility between Felodipine and the selected polymers. The pure drug and drug with excipients were scanned separately.

Drug-Excipient Compatibility Study by DSC [6]

Possible interaction of drug with various excipients to be used in prototype formulation was checked by using differential scanning calorimetry (DSC). DSC study of pure drug, proposed excipients and their combination used in prototype formulation was carried out using DSC instrument (DSC-60, Shimadzu, Kyoto, Japan). In this process, samples (3–5 mg) were put into aluminium cell and scanned at 50–300 °C, at 10°C per minute rate under nitrogen atmosphere against blank DSC aluminium cell as a reference.

Formulation design

Preparation of Oro dispersible film

Table-1: Formulation Design of Felodipine Oro dispersible film

RUN	Drug (mg)	HPMC E15(mg)	SSG (mg)	PEG 400 (mg)	DMSO (ml)	Aspartame (mg)
1	5	200	15	10	1	5
2	5	200	10	7.5	1	5
3	5	200	10	7.5	1	5
4	5	100	5	7.5	1	5
5	5	100	10	10	1	5
6	5	300	15	7.5	1	5
7	5	100	10	5	1	5
8	5	200	5	10	1	5
9	5	200	10	7.5	1	5
10	5	100	15	7.5	1	5
11	5	200	10	7.5	1	5
12	5	300	5	7.5	1	5
13	5	200	15	5	1	5
14	5	300	10	10	1	5
15	5	200	10	7.5	1	5
16	5	300	10	5	1	5
17	5	200	5	5	1	5

Solvent evaporation [7]

The orodispersible films were prepared using the solvent casting method. Accurately weighed HPMC E15 was dissolved in distilled water of under continuous stirring to form a clear viscous solution. The drug (5 mg) was then incorporated into the polymer solution, followed by the addition of the superdisintegrant (SSG), plasticizer (PEG 400), and sweetener (aspartame), ensuring thorough mixing to obtain a homogeneous solution. The resulting mixture was degassed to remove any entrapped air bubbles and then poured onto a clean, levelled petri dish or glass plate. The solution was spread uniformly and allowed to dry at room temperature or in a hot air oven at 40–50°C until a thin, transparent film was formed. The dried films were carefully peeled off and cut into the desired size, each containing the specified drug dose. The films were stored in airtight containers, protected from light and moisture, until further evaluation. Different runs were prepared by varying the amounts of HPMC, SSG, and PEG 400 according to the experimental design.

Evaluation of Oro dispersible films

Physical appearance[8]

All the prepared Oro dispersible film were observed for color, clarity, flexibility, and smoothness.

Thickness[9]

The thickness of the prepared orodispersible films was measured using a digital micrometre or vernier caliper. Films from each batch were randomly selected, and measurements were taken at three different points the centre and two opposite edges to account for any variability in casting. The average of these readings was calculated to represent the film thickness

Weight uniformity[10]

The weight uniformity of the prepared orodispersible films was evaluated by individually weighing 10 randomly selected films from each batch using a digital analytical balance. Each film was carefully handled to avoid tearing or damage. The individual weights were recorded, and the average weight was calculated. The deviation of each film from the average weight was determined to assess uniformity. This test ensures consistent dosing and quality, as variations in film weight can directly affect the drug content and therapeutic efficacy of the ODF.

Moisture absorption studies[11]

The moisture absorption of the prepared orodispersible films was evaluated by placing pre-weighed films (W_1) in a desiccator containing 75% relative humidity, typically maintained using a saturated solution of sodium chloride, at room temperature for a specified period, usually 7 days. After exposure, the films were removed and weighed again (W_2). The percentage moisture absorption was calculated using the formula:

$$\text{Moisture absorption (\%)} = W2-W1/W1\times100$$

The study helps to assess the hygroscopic nature and stability of the films under humid conditions, which is important for their mechanical integrity, disintegration, and drug release profile.

Moisture loss studies[12]

The moisture loss of the prepared orodispersible films was determined by first weighing pre-weighed films (W_1) and then placing them in a desiccator containing anhydrous calcium chloride at room temperature for a specified period, usually 7 days, to allow complete moisture removal. After the exposure period, the films were weighed again (W_2). The percentage moisture loss was calculated using the formula:

$$\text{Moisture loss (\%)} = W1-W2/W1\times100$$

This study helps to evaluate the drying stability and hygroscopicity of the films, which can influence their mechanical properties, flexibility, disintegration time, and overall shelf-life.

Folding Endurance[13]

The folding endurance of the prepared orodispersible films was evaluated by repeatedly folding a small strip of the film (approximately 2 × 2 cm) at the same place until it broke or showed visible cracks. The number of folds required to break the film was recorded as the folding endurance value. This test was performed on three randomly selected films from each batch, and the average value was calculated. Folding endurance is an important parameter that reflects the flexibility, mechanical strength, and handling properties of the films, which are critical for patient compliance and packaging.

Tensile strength[14]

The tensile strength of the prepared orodispersible films was evaluated using a tensile testing apparatus or universal testing machine. A film strip of standard dimensions (typically 2 × 6 cm) was clamped at both ends, and a gradual force was applied until the film broke or ruptured. The maximum force (F) required to break the film was recorded, and the tensile strength (TS) was calculated using the formula:

$$\text{Tensile Strength (TS)} = F/A$$

where F is the force at break (N) and A is the cross-sectional area of the film (m^2). Measurements were performed in triplicate, and the average value was reported. Tensile strength is an essential parameter that indicates the mechanical robustness, elasticity, and handling properties of the films, which are crucial for packaging, transportation, and patient use.

Drug content[15]

The drug content of the prepared orodispersible films was determined by dissolving a film of known weight in a phosphate buffer pH 6.8 under stirring until completely dissolved. The solution was then filtered to remove any undissolved excipients, and an appropriate dilution was made. The absorbance of the solution was measured using a UV-Visible spectrophotometer at the characteristic λmax of the drug. The drug concentration was calculated from a previously prepared calibration curve, and the percentage drug content was determined. The procedure was repeated for three randomly selected films from each batch, and the mean value was reported. This evaluation ensures uniform distribution of the drug within the films and confirms dose accuracy.

In Vitro Disintegration Time[16]

The in vitro disintegration time of the prepared orodispersible films was determined by placing a single film strip (approximately 2 × 2 cm) in a petri dish containing 10 ml of phosphate buffer pH 6.8 at room temperature. The time taken for the film to completely disintegrate into fine particles without any palpable film residue was recorded using a stopwatch. The test was repeated for three films from each batch, and the average disintegration time was calculated. This parameter is critical as it reflects the rapid dissolution and onset of action of the drug from the orodispersible film, which is a key characteristic of this dosage form.

In vitro dissolution study[17]

The in vitro dissolution of the prepared orodispersible films was performed using a USP type II (paddle) dissolution apparatus. A film containing a known amount of drug was placed in 900 ml of phosphate buffer pH 6.8 maintained at 37 ± 0.5°C with a paddle rotation speed of 50–100 rpm. At predetermined time intervals, 5 ml samples were withdrawn and replaced with an equal volume of fresh buffer to maintain sink conditions. The withdrawn samples were filtered, suitably diluted, and the drug concentration was determined using a UV-Visible spectrophotometer at the characteristic λmax of the drug. The percentage cumulative drug release was calculated using a standard calibration curve. This study provides information about the drug release profile, dissolution rate, and bioavailability potential of the orodispersible films.

Percentage of drug release was determined using the following formula.

$$\text{Perentage drug release} = \frac{\text{Da}}{\text{Dt}} \times 100$$

Where, Dt = Total amount of the drug in the film

Da = The amount of drug released

Drug release kinetics [18]

The drug release kinetics of the prepared orodispersible films were analyzed by applying the

in vitro dissolution data to various mathematical models to understand the mechanism of drug release. The cumulative percentage of drug released at different time intervals was fitted to models such as zero-order (drug release independent of concentration), first-order (drug release dependent on concentration), Higuchi (diffusion-controlled release), and Korsmeyer–Peppas (anomalous transport). The correlation coefficient (R^2) for each model was calculated, and the model with the highest R^2 value was considered the best fit, indicating the predominant mechanism of drug release from the film. This analysis helps in understanding whether the release is diffusion-controlled, erosion-controlled, or follows a combination of mechanisms, which is critical for designing films with predictable therapeutic performance.

Stability Study[19]

The stability of the prepared orodispersible films was evaluated by storing the films in airtight containers under controlled environmental conditions as per ICH guidelines. Films were stored at room temperature (25°C/60% RH) and accelerated conditions (40°C/75% RH) for a specified period, typically 1–3 months. At predetermined intervals, the films were withdrawn and evaluated for physical appearance, folding endurance and in vitro disintegration time, and in vitro drug release. Any changes in these parameters were recorded to assess the effect of storage conditions on the stability, mechanical integrity, and drug release profile of the films. The results help determine the shelf-life and optimal storage conditions for the orodispersible films.

3. RESULTS & DISCUSSION

Drug - excipient compatibility studies

Compatibility studies were performed using IR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and polymer were studied. The peaks obtained in the spectra of each formulation correlates with the peaks of drug spectrum. This indicates that the drug was compatible with the formulation components.

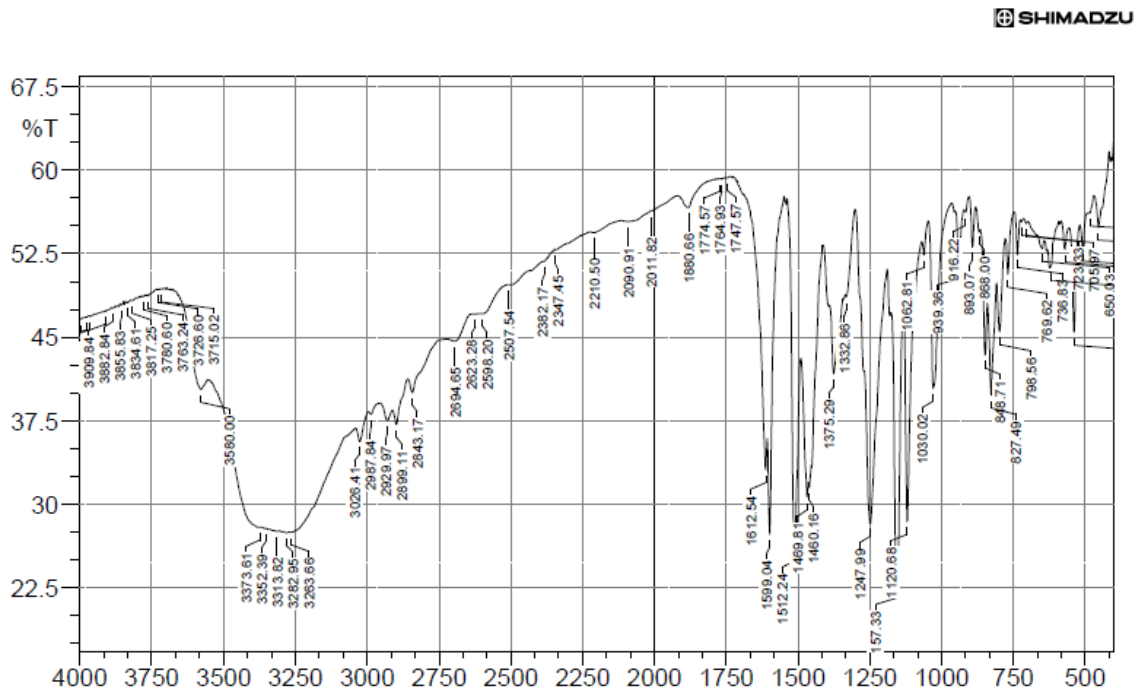

Fig-1: FT-IR Sample for Felodipine

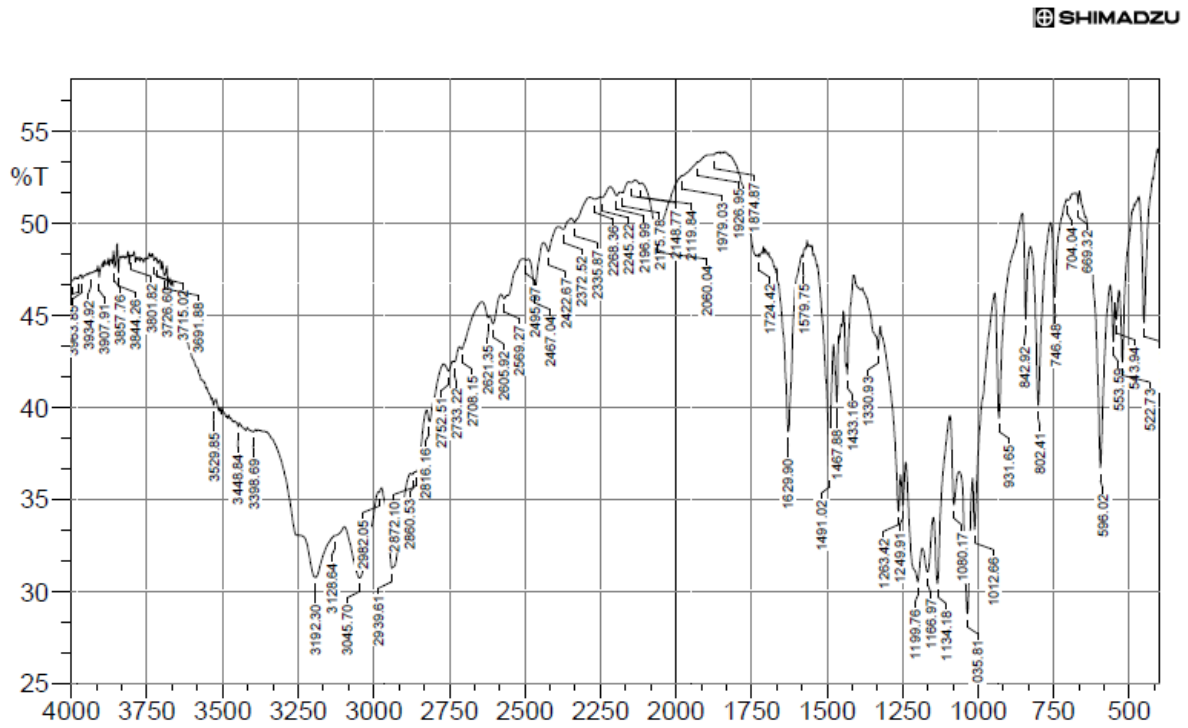

Fig-2: FT-IR Sample for Optimized Formulation

Compatibility studies were performed using IR spectrophotometer. The IR spectrum of Pure drug and physical mixture of drug and excipients were studied. The characteristic absorption of peaks were obtained as above and as they were in official limits (±100 cm^{-1}) the drug is compatible with excipients.

Evaluation of Oro dispersible films formulation

Weight Variation

The weight of the films ranged from 72.25 mg (F12) to 87.49 mg (F14), indicating slight variations across different formulations. These variations could be attributed to differences in polymer (HPMC E15) and plasticizer (PEG 400) concentrations, as higher polymer content generally increases the film weight. Despite minor variations, all films showed acceptable uniformity, ensuring consistent dosing.

Thickness

Film thickness varied from 0.15 mm (F1) to 0.53 mm (F9). Thicker films were observed in formulations with higher polymer and plasticizer concentrations, likely due to increased solution viscosity during casting. Thinner films, such as F1 and F14, may lead to faster disintegration, whereas thicker films could improve mechanical strength but slightly prolong disintegration time.

Folding Endurance

Folding endurance ranged from 206 (F9) to 263 folds (F6), reflecting the flexibility of the films. Films with higher PEG 400 content exhibited better folding endurance due to enhanced plasticization. Low folding endurance, as in F9, may indicate brittleness and potential handling issues. Overall, most films demonstrated adequate mechanical strength for practical handling.

Drug Content

Drug content ranged from 69.69% (F10) to 83.15% (F15). Formulations with lower drug content could result from uneven drug distribution during casting, particularly in films with

higher viscosity. Most films maintained acceptable content uniformity, ensuring accurate dosing.

Moisture Loss and Moisture Absorption:

Moisture loss values ranged from 6.17% (F6) to 6.74% (F2), while moisture absorption ranged from 7.12% (F11) to 8.30% (F15). These results indicate that the films are moderately hygroscopic. Formulations with higher polymer and superdisintegrant content tend to absorb slightly more moisture, which could affect mechanical properties and stability. Appropriate packaging is essential to minimize moisture-related changes.

Disintegration Time

Disintegration time varied significantly from 11 sec (F15) to 42 sec (F4). Faster disintegration was observed in films with higher superdisintegrant concentration and thinner films, facilitating rapid water penetration. Slower disintegration in thicker or more rigid films (F4) may be due to higher polymer content or lower superdisintegrant levels. Rapid disintegration is critical for patient compliance and rapid onset of action.

Tensile Strength

Tensile strength ranged from 5.93 MPa (F11) to 16.39 MPa (F7), reflecting the mechanical robustness of the films. Higher tensile strength was generally observed in thicker films or those with higher polymer content. However, excessive tensile strength can reduce flexibility and prolong disintegration, while lower tensile strength may lead to brittle films that are difficult to handle.

Table-2: Physicochemical evaluation of Felodipine oro dispersible films

F. code	Weight Variation (mg)	Thickness (mm)	Folding endurance	Drug content (%)	% Moisture loss	% Moisture absorption	Disintegration time (Sec)	Tensile strength (Mpa)
F1	75.82	0.15	253	79.68	6.39	7.59	25	7.1
F2	81.10	0.19	219	82.13	6.74	7.54	31	8.12
F3	79.86	0.21	246	76.39	6.25	7.86	28	7.56
F4	82.50	0.36	219	81.14	6.33	8.12	42	8.62
F5	75.63	0.49	248	78.10	6.29	7.56	27	15.28
F6	82.31	0.51	263	79.83	6.17	8.13	26	9.36
F7	86.90	0.46	249	71.16	6.20	8.10	32	16.39
F8	84.55	0.41	213	77.48	6.29	7.86	19	10.2
F9	79.86	0.53	206	80.32	6.35	7.82	36	9.68
F10	78.22	0.38	219	69.69	6.33	7.49	29	8.12
F11	83.36	0.32	225	71.32	6.55	7.12	35	5.93
F12	72.25	0.29	236	77.59	6.28	7.36	23	7.41
F13	83.36	0.27	248	78.55	6.19	7.58	17	7.28
F14	87.49	0.20	246	80.19	6.22	8.22	15	8.12
F15	86.39	0.36	237	83.15	6.32	8.30	11	6.38
F16	81.10	0.28	243	78.91	6.49	8.26	31	7.53
F17	80.26	0.20	259	81.25	6.22	8.29	25	11.25

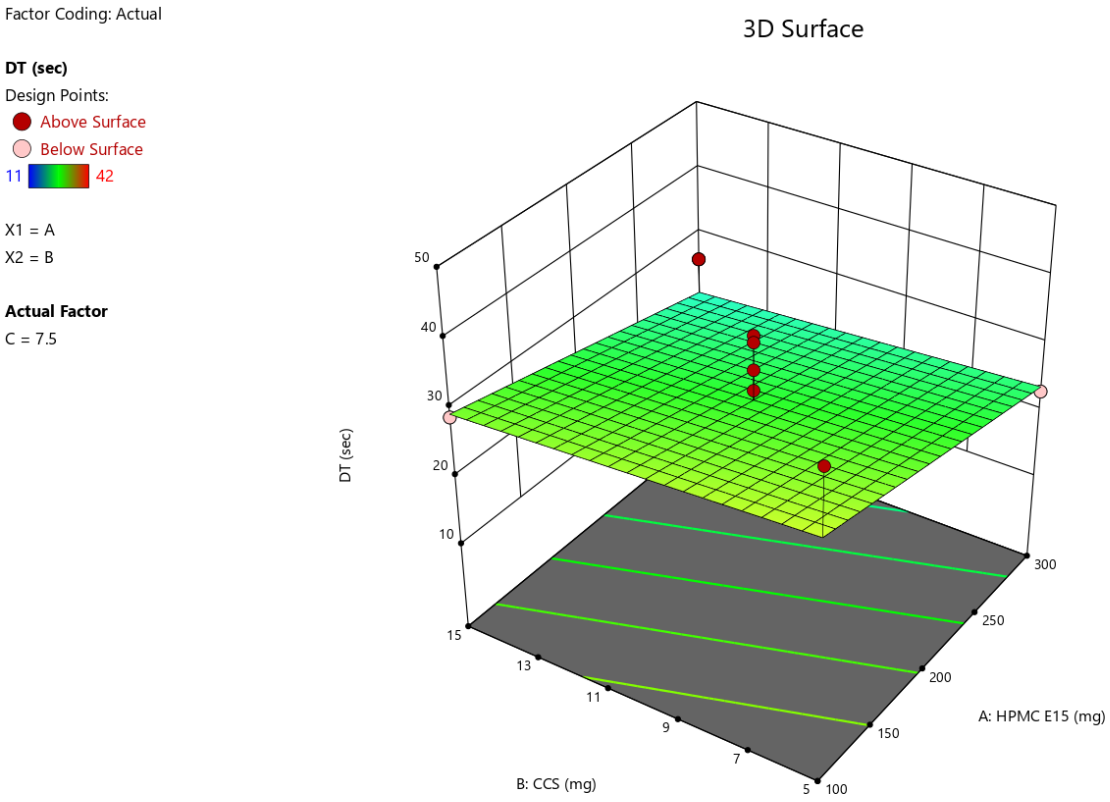

Fig-3: Response surface plot for disintegration time (DT)

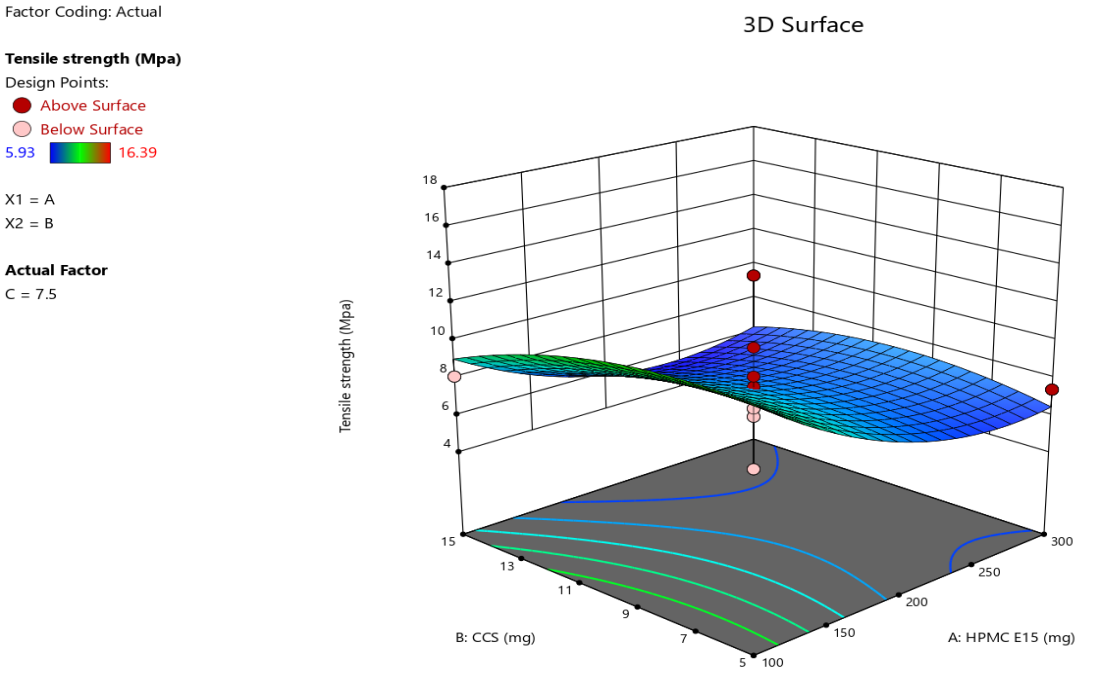

Fig-4: Response surface plot for Tensile strength (Mpa).

***In vitro* release study**

Table-3: *In vitro* drug release profiles of Felodipine Oro dispersible films (F1-F17)

Time	F15	Drug

(min)		solution
0	0	0
5	9.58	7.59
10	25.69	22.36
15	36.71	32.10
20	58.12	55.95
25	72.16	69.81
30	80.10	75.63

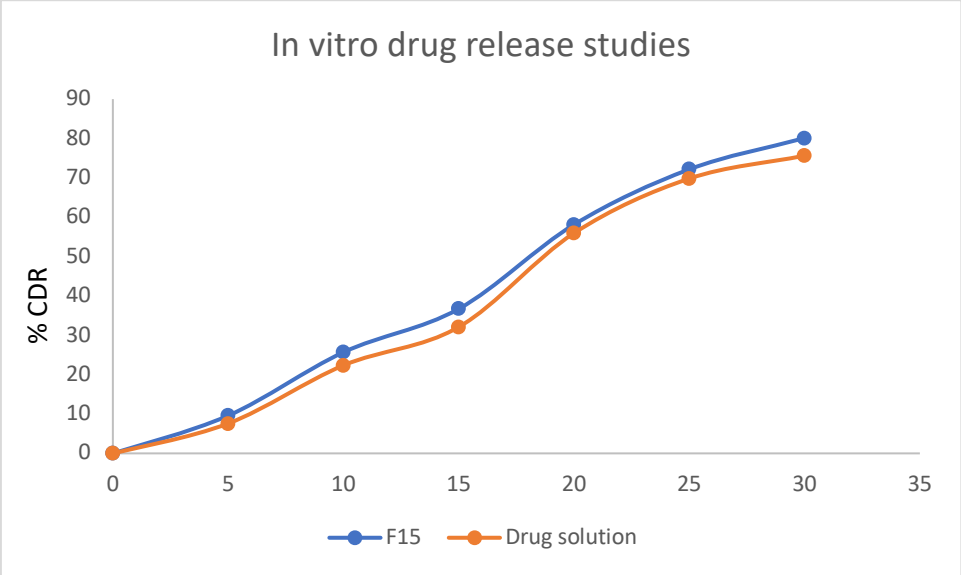

Fig-5: Drug release for Optimized formulation

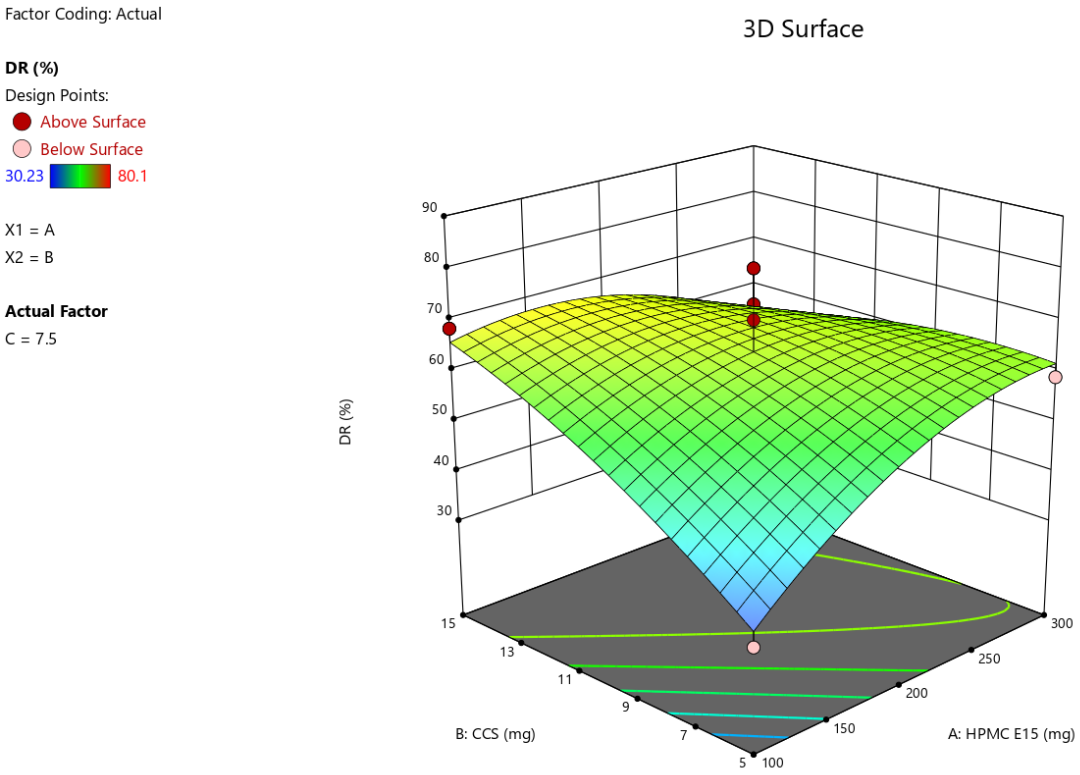

Fig-6: Response surface plot for Drug release studies (DR)

The in vitro drug release study of formulation F15 showed a rapid and progressive release of Felodipine over 30 minutes. The cumulative drug release increased from 9.58% at 5 min to 80.10% at 30 min, indicating effective dispersion and dissolution from the orodispersible film.

Kinetic models:

Table-4: Drug Release Kinetics of Formulation F15

Time (min)	%CDR	SQARE T	LOG T	LOG%CDR	ARA	LOG%ARA
0	0	0	0	0	0	0
5	9.58	2.23607	0.69897	0.9813655	90.42	1.84674
10	25.69	3.16228	1	1.4097641	74.31	1.81681
15	36.71	3.87298	1.17609	1.5647844	63.29	1.84436
20	58.12	5.47723	1.47712	1.7643256	41.88	1.77745
25	72.16	7.74597	1.77815	1.8582965	27.84	1.67169
30	80.1	10.9545	2.07918	1.9036325	19.9	1.63349

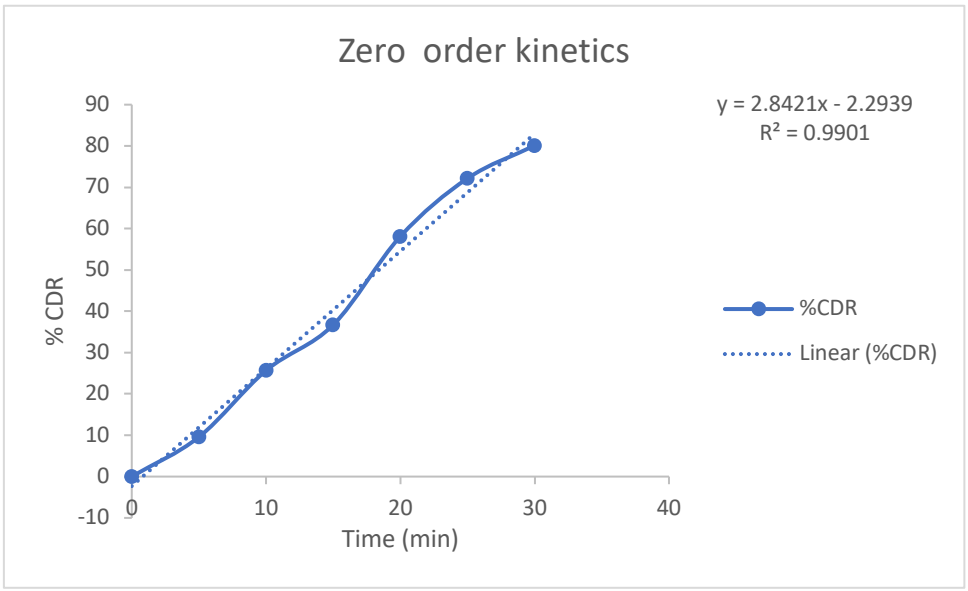

Fig-7: Zero order kinetics of optimized formulation

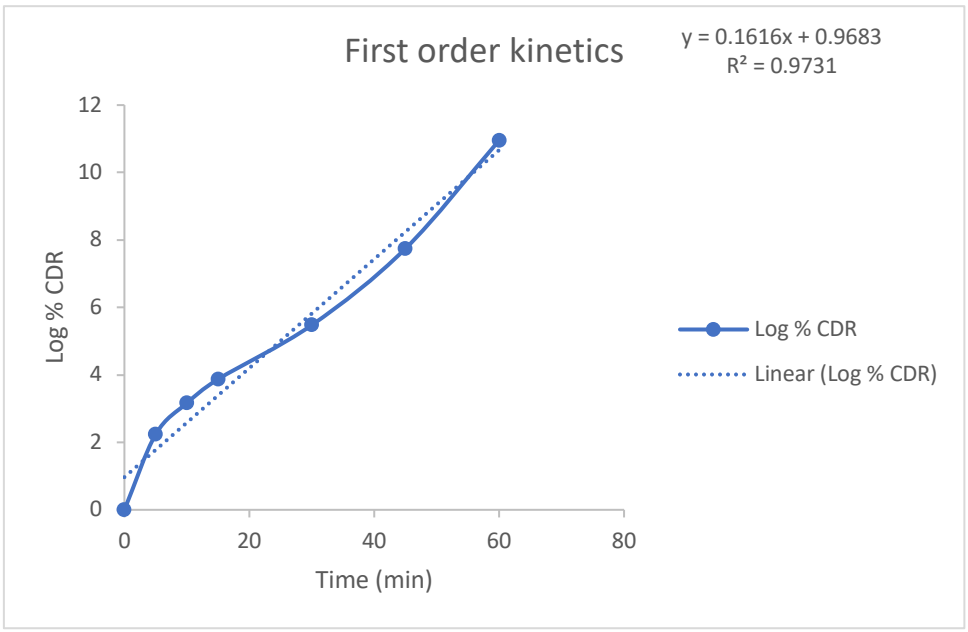

Fig-8: First order kinetics of optimized formulation

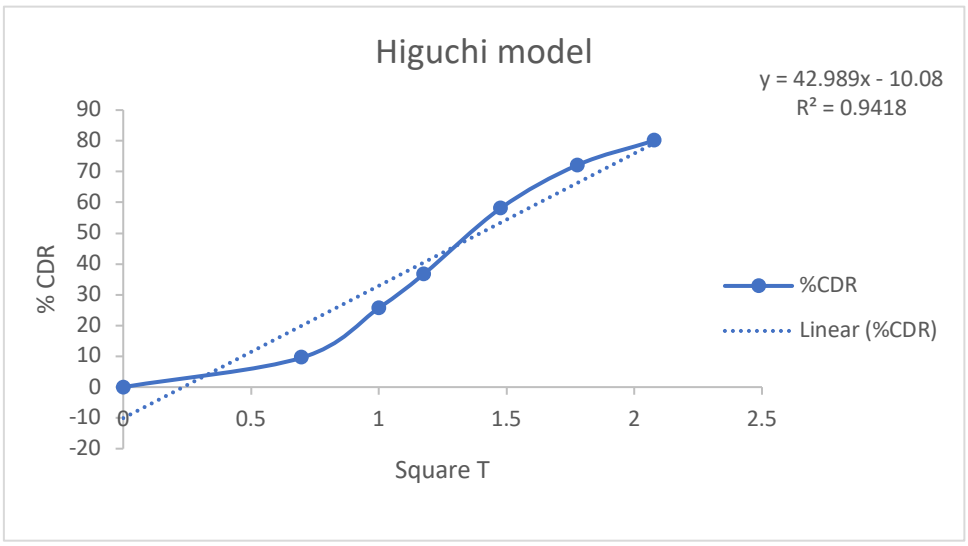

Fig-9: Higuchi model of optimized formulation

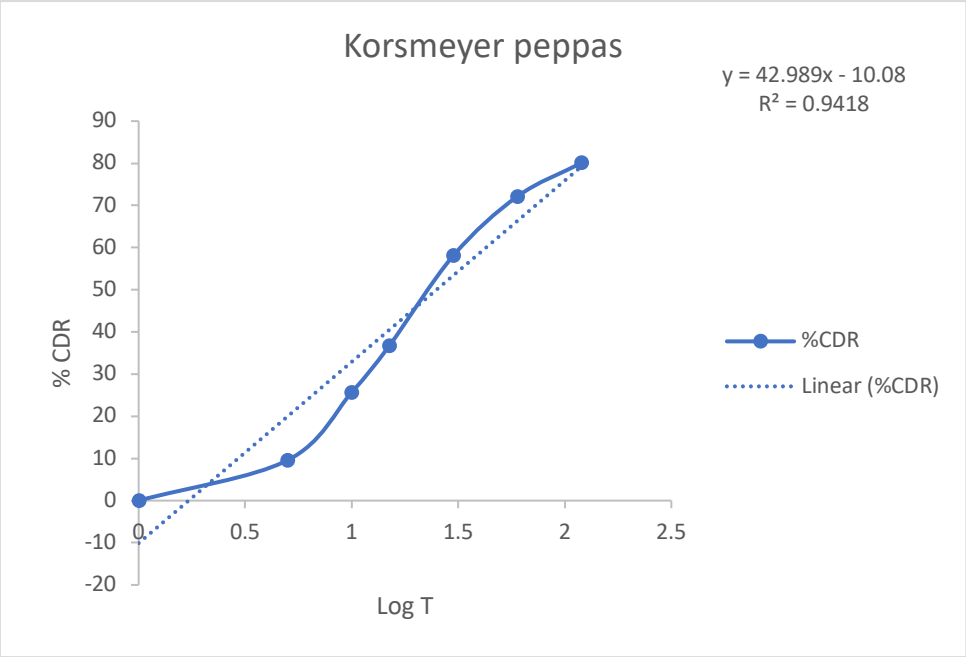

Fig-10: Korsmeyer peppas of optimized formulation

Stability studies

There was no significant change in physical and chemical properties of the oro dispersible films of formulation F-15 after 90 days. Parameters quantified at various time intervals were shown.

Table-5: Stability studies of all formulations

F.no	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-15	25^{0}C/60%RH % Release	80.10	79.86	78.50	77.52	Not less than 85 %
F-15	30^{0}C/75% RH % Release	80.10	79.15	78.55	77.15	Not less than 85 %
F-15	40^{0}C/75% RH % Release	80.10	79.89	78.46	77.60	Not less than 85 %

4. CONCLUSION

In the present study, Felodipine orodispersible films were successfully formulated using the solvent casting method with HPMC E15 as the film-forming polymer, SSG as a superdisintegrant, PEG 400 as a plasticizer, and aspartame as a sweetener. Drug-excipient compatibility studies using FTIR were no significant interactions between Felodipine and the selected excipients, indicating the suitability of the formulation components. The physicochemical evaluation of the films demonstrated acceptable weight uniformity, thickness, folding endurance, tensile strength, and drug content, indicating good mechanical integrity and dose accuracy. Moisture absorption and loss studies revealed that the films were moderately hygroscopic but stable under controlled conditions. Disintegration studies showed rapid disintegration, with F15 exhibiting the fastest disintegration time (11 sec), confirming its suitability for orodispersible delivery. In vitro dissolution studies demonstrated that formulation F15 provided a rapid and progressive drug release, achieving 80.10% release

within 30 minutes, closely matching the release profile of the drug solution. Drug release kinetics indicated that the release from F15 followed a diffusion-controlled mechanism, as suggested by Higuchi and Korsmeyer–Peppas models. Stability studies conducted at various temperature and humidity conditions for 90 days showed no significant changes in physical appearance, mechanical properties, or drug release, indicating that the films were stable and suitable for further development. Overall, formulation F15 was identified as the optimized formulation, exhibiting rapid disintegration, adequate mechanical strength, uniform drug content, and favourable drug release characteristics, making it a promising candidate for improved oral delivery of Felodipine with enhanced patient compliance and therapeutic efficacy.

5. REFERENCES

1. Fini A, Orodispersible films: A new approach to oral drug delivery. J Control Release. 2008;126:179–185
2. Chandrasekaran R, FTIR and DSC analysis in drug-excipient compatibility studies. Int J Pharm Pharm Sci. 2014;6(8):123–129.
3. Verma S, Formulation and evaluation of fast dissolving films. Int J Pharm Sci Rev Res. 2010;3(2):22–27.
4. Sreenivas SA, Development and evaluation of oral thin films. J Pharm Sci. 2012;101:3745–3752.
5. Gunda, R.K.; Kumar, J.N.S. Formulation Development and Evaluation of Amisulpride Fast Dissolving Tablets. FABAD J. Pharm. Sci. 2018, 43, 105-15.
6. Bhatt, Shailendra.; Mandge, Shailendra.; Jaimini, Manish.; Tanwar, Yuveraj.; Trivedi, Priti. Design and optimization of Domperidone Fast Dissolving Tablets using central Composite Design. Cur. Drug Del. 2015, 12, 736-44,
7. Sambasiva, Rao, M.; Sunil,Reddy.; Ashok ,A. Formulation development and characterization of fast disintegrating tablets of felodipine. Indo Amer. J. pharm. Sci. 2016, 3, 135-141,
8. Santosh, Kumar,K.; Bhavani, B.; Vijaya, Ratna, J. Formulation and Evaluation of Fast Dissolving Tablets of Felodipine. Int. J. Eng. Res. Tech. 2012, 1, 1-16.
9. Tapas, A.R.; Kawtikwar,P.S.; Sakarkar, D.M. Enhanced dissolution rate of felodipine using spherical agglomeration with Inutec SP1 by quasi emulsion solvent diffusion method. Res. Pharm. Sci. 2009, 4, 77- 84.
10. Gunda, R.K.; Manchineni, P.R. Statistical Design and Optimization of Sustained Release Formulations of Pravastatin. Turk. J. Pharm. Sci.. 2020, 17, 221-227,
11. Gupta S, Evaluation parameters for orodispersible films. Int J Drug Dev Res. 2013;5(3):45–53.
12. Korsmeyer RW, Mechanisms of solute release from porous hydrophilic polymers. Int J Pharm. 1983;15:25–35.
13. ICH Q1A(R2). Stability testing of new drug substances and products. International Conference on Harmonisation, 2003.
14. Hoffmann EM, Breitenbach A, Breitkreutz J. Advances in orodispersible films for drug delivery. Expert Opin Drug Delivery 2011;8:299-316.
15. Misra R, Amin A. Formulation development of taste-masked rapidly dissolving films of citrizine hydrochloride. Pharm Technol 2009;33:48-56.

16. Vasantha PV, Puratchikody A, Mathew ST, Balaraman AK. Development and characterization of Eudragit based mucoadhesivebuccal patches of salbutamol sulfate. Saudi Pharm J 2011;19:207-14.
17. Hema Chaughary, Samita Gauri, Permender Rathee, Vikash Kumar. Development and optimizationof fast dissolving orodispersible films of granisetron HCl using Box-Behnken statistical design. Bull Faculty Pharm Cairo University 2013;51:193-201.
18. Hill SW, Varker AS, Karlage K, Myrdal PB. Analysis of drug content and weight uniformity for half-tablets of 6 commonly split medications. J Manag Care Pharm 2009;15:253-61.
19. Raju S, Sandeep Reddy P, Anirudh Kumar V, Deepthi A, Sreeramulu Reddy K, Madhava Reddy PV. Flash release oral films of metoclopramide hydrochloride for pediatric use: formulation and in vitro evaluation. J Chem Pharm Res 2011;3:636-46.