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FORMULATION AND EVALUATION OF MODIFIED RELEASE BILAYER ORAL STRIPS OF PREGABALIN TO TREAT EPILEPSY

PATEL P[1], PRAJAPATI B[*2] AND PATEL D[3]

1: Research Scholar, Department of Pharmaceutics, Shree S.K.Patel College of Pharmaceutical Education and Research, Ganpat University, Gujarat,384012 India

2: Department of Pharmaceutics, Shree S.K.Patel College of Pharmaceutical Education and Research, Ganpat University, Gujarat,384012 India; **ORCID ID:** https://orcid.org/0000-0001-8242-4541

3: Asst. Professor, Department of Pharmacology, Ananya College of Medicine and research Kalol

***Corresponding Author: Dr. Bhupendra Prajapati: E Mail:** bhupendra.prajapati40731@paruluniversity.ac.in

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ABSTRACT

The bilayer oral strip is a suitable and pleasant delivery method, facilitating easy administration for pediatric patients. Pregabalin, acting on voltage-gated calcium channels and specifically binding to the α2-δ subunit, was explored for formulating such a strip. With each layer disintegrating rapidly, the first layer aims for immediate drug release to swiftly alleviate neuropathic pain (characterized by burning and shooting sensations), while the second layer provides sustained release to prevent recurrent attacks for a specified duration. Utilizing casting and double casting techniques ensured that the bilayer film exhibited the essential both physical and mechanical attributes. Various plasticizers were mixed with a spectrum of hydrophilic and hydrophobic polymers in varying ratios and concentrations. Their impacts on variables including mechanical characteristics, in-vitro disintegration time, and release profile were thoroughly investigated. The optimized formula (F5) demonstrated a disintegration time of 25 seconds, releasing 90% of the drug within the initial 6 minutes, followed by sustained release for up to 3 hours. The quick release profile and the commercially available oral Pregabalin tablet were compared. The film remained stable for 3 months as per ICH Q1A (R2) guidelines. In an in vivo study with rats, the drug's bioavailability increased 663.9-fold and reached systemic circulation within 15 minutes.

Keywords: Child-appropriate dosage form, Pregabalin, Oral Bilayer Film, Sustained Release, factorial design, In vitro Release kinetics study, stability study, in vivo animal study

INTRODUCTION:

Mouth dissolving films, or oral wafers, are thin oral strips that quickly wet with saliva, disintegrate, and release medication for mucosal absorption **[1, 2]**. Introduced in the late 1970s, the quick-dissolving medication delivery method has revolutionized treatment options for noncompliant, elderly, and pediatric patients. Oral disintegrating films (ODFs), which incorporate various water-soluble medications, are promising for oral administration as they dissolve rapidly and do not require water for swallowing **[3]**. They come in flash-release, Mucoadhesive melt-away, and sustained-release types, ranging from 2-8cm^2 and 20-500µm thick, with flexible compositions of water-soluble hydrophilic or low/non-soluble polymers **[4]**. Fast-release wafers dissolve in 60 seconds, instantly releasing drug; Mucoadhesive melt-away wafers adhere and continuously release drug; Mucoadhesive sustained-release wafers offer prolonged adherence for flexible dosing, particularly suitable for pediatric populations **[5, 6]**. Advanced oral solid dose forms include fast-dissolving oral films. rapidly dissolving in the oral cavity upon saliva contact, improving drug bioavailability without chewing or water **[7, 8]**. A bilayer oral strip formulation includes strip-forming components, APIs like Pregabalin, sweeteners, flavouring, and enhancers. Pregabalin, binding to alpha-2-delta subunit of calcium channels, treats epilepsy, neuropathic pain, and fibromyalgia, with convenient pediatric ODF dosage. Pregabalin, also known as (S)-(+)-3-aminomethyl-5-methylhexanoic acid, is linked to the inhibitory neurotransmitter GABA and binds to the alpha-2-delta subunit of calcium channels. It treats epilepsy, neuropathic pain, and fibromyalgia, with recommended doses of 10, 25, or 75 mg once or twice daily for children aged 5-16 years. Currently, pediatric doses are administered via capsules that must be mixed with soft food **[9]**. Oral disintegrating films (ODFs) could offer a more convenient alternative **[10]**. Pregabalin is a prismatic solid with a bitter flavor, with a melting point about 176 and 178°C, and a solubility of 11.3 mg/mL. Its completely saturated state has a pH of 6.3, and its half-life is 5–6 hours. Classified as a Class I drug by the biopharmaceutical classification system, Pregabalin has high solubility and permeability **[11]**. The rationale for mouth dissolving film development is to enhance drug bioavailability and bypass first-pass metabolism, suiting epilepsy treatment in children, with Pregabalin properties facilitating its effectiveness **[12]**. Formulation of immediate / prolonged release oral dissolving films with potential for drug delivery in children depending on

the drug loading capacity, using different grade polymer, disintegration time.

MATERIAL AND METHOD

Materials

Pregabalin, βCyclodextrin, Glycerol anhydrous, Propylene Glycol, PVA, Hydroxypropyl methylcellulose E3, E5, E15, ethyl cellulose, PVP, Eudraget RS 100, Sucralose, Eco cool, citric acid, chocolate flavour, Mannitol, absolute HPLC grade ethanol was acquired from SCION PHARMA PVT. LTD. Every experiment utilized distilled water. As supplied, all chemicals were utilized.

Experimental factorial design

The formulation preparation utilized a factorial design with two factors and three levels. The amount of polymer used was set at low, medium, and high levels. For HPMC E15, the low level was 0.25 g, the medium level was 0.30 g, and the high level was 0.35 g. For glycerol anhydrous, the low level was 1 ml, the medium level was 1.5 ml, and the high level was 2.0 ml **[13]**.

Calculating Dosage (Amount of Drugs to pour on each Plate)

Plate Diameter = 6 cm.

Plate Area = πr^2 = 3.14*9=28.26 cm^2

4 cm2 films present in entire plate = 28.26/4 = 7.065 films

Each film has a dosage of 25mg of PGB

The quantity of drug put onto each plate was = 7.065 * 25 = 176.6mg

Methods

Preparation of fast dissolving layer

Fast-dissolving film formulations **(Table 1)** were prepared using the solvent casting technique. In a 50 ml beaker, dissolve the water-soluble film-forming ingredients and plasticizers in hot distilled water. Using a magnetic stirrer, stir at 150 rpm for two hours. After using a sonicator to eliminate air bubbles, remove the solution and set it aside. In separate vessel take specified quantity of water and dissolve resulting solid dispersion Pregabalin Super disintegrate into it, after that add salivary agent, sweetening agent and Stir the mixture for 30 minutes at 150 rpm using a magnetic stirrer. To make the initial film layer, combine both solutions and cast into a Petri dish. Dry for one hour at 60°C in a hot air oven **[14]**.

Development of sustained Release layer

Casting a sustained release layer on top of a quick release layer produced bilayer strips **(Table 2)**. Dissolve the film-forming agent and plasticizer for the sustained release layer in distilled water, stir for 2 hours at 150 rpm to ensure homogeneity and remove air bubbles. Dissolve excipients and medicine in pure water, stirring constantly for 30 minutes. Combine both solutions and cast onto the fast release layer (F5) in a Petri dish. After an hour of drying at 60°C, peel and gather the bilayer film. Each strip contained 50 mg of Pregabalin, with 25 mg in each layer **[14]**.

Physico-chemical Characterization

Film thickness was measured at five positions using a screw micrometre, with results reported as mean ± standard deviation **[15, 16]**. Weighing was used to establish the weight of the film, also reported as mean ± standard deviation **[17]**. To determine the surface pH, the film was soaked for two hours at room temperature in one millilitre of pH 7.4 phosphate buffer, then measured using electrodes **[15]**.

The film was folded 300 times in the same spot to test its durability before it broke **[15, 18]**. Maximum stress applied to the point at which the strip specimen breaks was used to assess tensile strength. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip **[19, 20]**.

By dissolving a film containing 50 mg of Pregabalin in a phosphate buffer (pH 7.4), the amount of Pregabalin in the film was found. Then, using a UV spectrophotometer set to its maximum wavelength, the Pregabalin content was determined. Pregabalin% content of the active component is computed as the drugs content in the film divided by the drug's addition quantity, expressed as a percentage **[13, 21]**. The disintegration test used the Petri dish method. Put one film on the surface of 2 millilitres of distilled water in a Petri dish. Record the time taken for the film to dissolve completely **[20, 22]**.

Pregabalin assay

Pregabalin content was analysed using a validated HPLC method per ICH Q2 guidelines. The phosphate buffer (pH 7.4) and acetonitrile made up the mobile phase. The HPLC system (Shimadzu LC-2010 AVP or equivalent) used a C18 column (4.0 mm × 25 mm, 5 µm) and ran at 1.0 ml/min. Twenty microliters of drug-loaded film samples, each measuring six centimetres, were injected after being diluted in ten millilitres of the mobile phase and passing through a 0.45 micrometre polypropylene filter. Absorption was measured at 485 nm **[23-27]**.

In vitro Drug Release

An ODF formulation's release profile was assessed utilizing a USP Type II (paddle) dissolving device. The film with Pregabalin was immersed in 900 mL of phosphate buffer (pH 7.4) at 37 ± 0.5°C, with the paddle set to 100 rpm. At 1, 2, 3, 5, 6, 7, 8, 9, and 10 minutes, Samples containing 5.0 mL were removed and replaced with fresh buffer **[28]**. The samples were passed over a 0.45 µm membrane filter and measured at 485 nm. The procedure was done in triplicate **[20, 29]**.

Analysis of Data

The release study analysed using the release kinetics model (Zero order, First order, Higuchi, Korsmeyer peppas) and mechanism.

Stability study

The improved Bilayer dissolving film composition underwent an expedited stability analysis to evaluate its chemical and physical stability **[30]**. Every film sample (3 cm × 2 cm) was individually wrapped in aluminium foil and kept for three months at (40°C ± 2°C / 75% ± 5% RH). Each Bilayer dissolving film sample was evaluated for Pregabalin tensile strength, breck-down time, and % cumulative drug release, % Drug Content **[20, 31]**.

In Vivo animal study

Male Inbred Wistar rats (250-330 g) were used in the study, approved by the CPCSEA Ethical Committee (DL/IAEC/DIPS/09/2024/87). The study was conducted at Deshpande Laboratories Pvt. Ltd., an ISO 9001:2008 certified drug testing laboratory. Animals were given a standard pellet diet ad libitum and kept in a noise-controlled environment with a 12-hour light/dark cycle. Test samples (6 cm^2, 50 mg) were applied to the buccal mucosa with a blunt spatula for 15 minutes, ensuring they were not displaced or ingested. Blood samples were collected via orbital puncture at 5, 10, and 15 minutes post-application and the serum separated by centrifuging them for ten minutes at 1500 rpm.

HPLC analysis

Plasma was precipitated with 1:1 methanol, and the supernatant was analyzed by HPLC. The analysis used RP-HPLC on a BDS Hypersil C8 column with a mobile phase of methanol: Water

(20:80, v/v), a flow rate of 1.0 mL/min, and UV detection at 402 nm, with a retention time of 5.8 minutes **[32]**.

Pharmacokinetic Characteristics

The pharmacokinetic Characteristics examined included single-dose measurements at three time points, with t (min) vs. AUC analyzed from chromatograms using Excel. The pharmacokinetics of the optimized test sample, API, and marketed Gabawin (50 mg tablet) were assessed. Pregabalin concentration in the blood was determined using RP-HPLC.

RESULT AND DISCUSSION

Fast Dissolving Layer

Optimization of formulation

The independent variable in this research were Glycerol anhydrous (ml) (X1) And HPMC E15 (gm) (X2) while the dependent variable were strength of elasticity (Y1), a break-down (Y2), and a % cumulative drug release (Y3). The strength of elasticity, a break-down, and % cumulative drug release were analyzed using design expert software, version 13 to obtain the following equation (1), (2), (3):

Tensile strength (Y1), $= 2.24 - 0.0300\ X_1 - 0.5100\ X_2 - 0.0550\ X_1\ X_2 + 0.3067\ X_1\ X_1 + 0.3867\ X_2\ X_2$. ….. (1)

Disintegration Time (Y2), = 72.80 + 2.75 X_1 – 40.88 X_2 – 3.39 X_1 X_2 + 14.04 X_1 X_1 – 3.85 X_2 X_2 …..(2)

% cumulative drug release (Y3) = 92.88 – 1.25 X_1 + 5.11 X_2+ 0.12 X_1 X_2 – 2.50 X_1 X_1 – 2.84 X_2 X_2 …. (3)

Where X1= amount of Glycerol anhydrous (ml) and X2 = amount of HPMC E15 (gm)

The contour plot of a strength of elasticity, a break-down, and % cumulative drug release is shown in **Figure 1**. Red in the contour map denotes the highest expected reaction, and blue the lowest.

The optimum area is an outcome of a plot overlaying a strength of elasticity, a break-down Time, and % cumulative drug release **Figure 1**. Optimal region generated by superimposing the 1.76 ml Glycerol anhydrous plasticizer and 0.373 gm HPMC E15 polymer are used. The optimum formula F5, which contains 1.5 ml glycerol anhydrous plasticizer and 0.30 gm HPMC E15 polymer, was selected based on its performance in Tensile strength, Disintegration Time and Percent drug release. This selection was made from the attractiveness study, overlay study, and other assessments of the factorial design clusters.

Evaluation of factorial design batches

The region that met the ideal criteria is shown in this plot. The primary response shapes were overlaid on a structural plot to create this composite overlay. The plot visually represents the zone of desirable response values within the variable space.

The projected and observed values are nearly identical due to the well-designed data points: Tensile strength (2.03±0.58), disintegration time (25.26±0.58), and percent drug release (92.25±3.18). Thus, this batch is considered optimized and was chosen to produce mouth-dissolving film.

Table 3 results demonstrate that the selected polymer and plasticizer concentrations result in the Thickness of the film, Excellent mechanical qualities (folding endurance above 200/tensile strength), and surface pH that is within the oral cavity's standard physiological range **[33]**.

Comparing the rapid release layer's specified disintegration release profile formulation F5 with the marketed Pregabalin oral dispersible tablet (Pregalin), **Table 3** results demonstrate that the cumulative percentage of Pregabalin release is similar between the makes formula F5 and the sold Pregabalin edible tablet (Pregalin), as illustrated **Figure 2**.

Sustained Release Layer

Physical Properties

Formulas F1 to F10 were used to examine how polymer type (Eudragit RS 100, Ethyl cellulose, PVP K30), content and combining ratios affect on the PGB (Pregabalin) bilayer strip Physical attributes.

The results in **Table 4** for Formulas F1 to F5, prepared by combining Eudragit RS 100 and PVP K30 in different ratios, showed that disintegration time increased as the concentration of Eudragit increased and PVP decreased **[34]**. This results from the aquatic polymer PVP K30's swelling feature, which creates a gel-like layer that slows disintegration and decreases water penetration.The swelling effect becomes more pronounced with higher concentrations of the hydrophilic polymer **[35, 36]**.

In contrast, for formulas F6 to F10, which combined ethyl cellulose and PVP K30 in different ratios, PVP K30 was added, and this shortened the disintegration time.

The drug content (%) of F1 to F10 result showed in **Table 4** respectively. A low drug content value indicates a very small proportion of the drug relative to the excipient **[37]**.

In vitro released profile of the drug (Pregabalin) is released from both the fast-release and sustained-release layers, in Phosphate buffer pH 7.4 at 37 ^{0}C.

In the combination of Eudragit RS 100 with PVP K30, the release data for F5 showed 50% drug release in 100 minutes. In contrast, other formulas (F1 to F4) that also combined Eudragit with PVP took longer to release the first 50% of the drug. This is due to the gelling effect of PVP in the sustained-release layer, which impacts the drug release from the fast-release layer **[38]**. For the combination of ethyl cellulose with PVP K30, the release data for F10 showed 50% drug release in 80 minutes. This is due to the lower disintegration time in these formulas compared to the Eudragit-based ones, indicating that the sustained-release layer with ethyl cellulose has a lesser impact on drug release from the fast-release layer, as illustrated in the **Figure 3**.

Optimized formula F10 sustained layer composed form ethyl cellulose, lowest disintegration time (32 sec) and released the remaining drug is released in a sustained and consistent manner over 180 minutes.

Analysis of the release kinetics model and mechanism

A release exponent (n) of 0.7896 indicates the diffusion process is strongly coupled to the mechanical response of the polymer with time-dependent, first-order release, where drug release involves both polymer diffusion and erosion. With an n value of 1.0538, the release is swelling-controlled and follows a zero-order process, independent of time **[13]**.

Pregabalin shows zero-order, first-order, and Higuchi release kinetics in bilayer oral films with HPMC E15 and ethyl cellulose. The combination of these polymers can retard drug release, resulting in a diffusion-sustained mechanism **[13, 39, 40]**. This indicates that the polymers used

significantly influence the drug's release kinetics, as shown in **Figure 4**.

Stability study

Bilayer Sample stored at(40^0 C ± 02^0C / 75 % ± 5% RH) and the initial condition did not reveal any changes in Tensile strength, Disintegration Time (Sec), % CDR, Drug content. In stability studies results show in **Table 5**, the increased lag time suggests the potential for drug and polymer moisturizing reactions during the study period. However, the Tensile strength, Disintegration Time, Dissolution profile and drug content of the film forming product has had very little effect. No significant change was observed in the all Parameter of drugs before and after 3 month stability studies.

Pharmacokinetic study

Figure 5 shows the AUC for Pregabalin API, the Pregabalin test sample, and Gabawin-50, plotted against plasma concentration over time (min) in male Inbred Wistar rats. The data, analyzed using Excel, were based on a single dose administered at three time points. The pharmacokinetics of the developed bilayer film were evaluated by buccal mucosal administration. Compared to the API and marketed tablet, the drug achieved plasma concentration within 15 minutes. The AUC values were 14248 mAU for the test film, 2624 mAU for the API, and 2146 mAU for the marketed product. The test film showed a significantly higher AUC, indicating a 663.9-fold increase in relative bioavailability compared to the marketed product.

Table 1: Quantitative composition of the casting solution for drug + β- Cyclodextrin load (25 mg) and the development of a fast-disintegrating film, including ingredients (SSG 0.075gm, Citric acid 0.070gm, Sucralose 0.050gm and water up to 10ml)

Formula Code	Glycerol anhydrous (mg)	HPMC E15 (gm)
F1	1000	0.25
F2	1500	
F3	2000	
F4	1000	0.30
F5	1500	
F6	2000	
F7	1000	0.35
F8	1500	
F9	2000	

Table 2: Composition of the double casting solution for the Pregabalin + β- Cyclodextrin loaded 25 mg sustained-release Layer Cast on the F5 fast-release layer [ingredients (HPMC E15 1.5 gm, Glycerol anhydrous 0.30 ml SSG 0.075gm, Citric acid 0.070gm, Sucralose 0.050gm and water up to 10ml)] and developed of a Bi-Layered Pregabalin Oral Strip, ingredients (HPMC E15 0.362 gm, Glycerol anhydrous 1.74ml)

Formulation No.	Second Pregabalin Sustained release layer		
	Eudraget RS 100 (mg)	Ethyl cellulose (mg)	PVPk30 (mg)
F1	12.5	-	12.5
F2	15	-	10
F3	17.5	-	7.5
F4	20	-	5
F5	25	-	0
F6	-	12.5	12.5
F7	-	15	10
F8	-	17.5	7.5
F9	-	20	5
F10	-	25	0

Table 3: Evaluation of mouth dissolving film selected batch F5 and Comparison of optimized MDF batch F5 % Drug release with conventional marketed product (Pregalin) formulation % Drug release

Evaluation of mouth dissolving film selected batch F5		Comparison of optimized MDF with conventional marketed formulation		
Evaluation parameter	Results	Time (min)	% Drug release (F5)	% Drug release of marketed product (Pregalin)
Thickness (mm)	0.15±0.02	0	0	0
Surface pH	6.7±0.04	1	14.75±0.13	0.264±2.12
Folding Endurance	299.25±1.15	2	34.3±1.78	6.274±0.17
		3	46.22±1.68	10.31±0.12
		4	62.9±1.26	43.22±1.21
		5	87.95±1.59	56.18±1.31
		6	94.86±0.15	67.46±1.12

***Results are presented as mean ± standard deviation (S.D.), n=3**

Table 4: Physical Properties

Formulation code		Film Thickness (mm)	In-Vitro DT(Sec)	Surface pH	Drug Content (%)	TS (N/mm2)	Folding Endurance
Eudraget RS 100 :PVP k30	F1	0.108 ±0.001	97 ±0.023	6.1 ±0.001	87.02 ±0.48	2.407 ±0.3	196
	F2	0.144 ±0.001	95 ±0.012	5.9 ±0.002	87.20 ±0.52	2.347 ±0.20	202
	F3	0.131 ±0.001	84 ±0.017	6.2 ±0.001	86.63 ±0.32	2.300 ±0.30	255
	F4	0.152 ± 0.001	59 ±0.024	6.2 ±0.001	89.60 ±0.48	1.545 ±0.30	265
	F5	0.124 ±0.001	133 ±0.011	6.2 ±0.001	89.73 ±0.64	2.470 ±0.25	299
Ethyl cellulose : PVPk30	F6	0.104 ±0.001	46 ±0.028	6.1 ±0.002	88.50 ±0.39	2.347 ±0.20	321
	F7	0.108 ±0.001	47 ±0.039	5.9 ±0.001	85.30± 0.54	2.300 ±0.30	346
	F8	0.108 ±0.001	51 ±0.012	5.9 ±0.001	95.96 ±0.53	2.545 ±0.30	375
	F9	0.107 ±0.001	53 ±0.013	6.3 ±0.002	94.30 ±0.47	2.470 ±0.25	375
	F10	0.161 ±0.001	32 ±0.015	6.3 ±0.003	97.63 ±0.40	2.715 ±0.30	394

***Results are presented as mean ± standard deviation (S.D.), n=3**

Table 5: Stability study

Parameter	Initial*	After 3 month*
	(40^0 C ± 02^0C / 75 % ± 5% RH) Storage condition	
Appearance	Very good	Very good
Tensile strength(N/cm^2)	2.715 ±0.30	2.72±0.3
Disintegration Time(Sec)	32±0.015	32.30±0.013
% CDR	98.8±0.13	97.3±0.32
% Drug Content	99.52±00.29	99.15±00.10

*** Results are presented as mean ± standard deviation (S.D.), n=3**

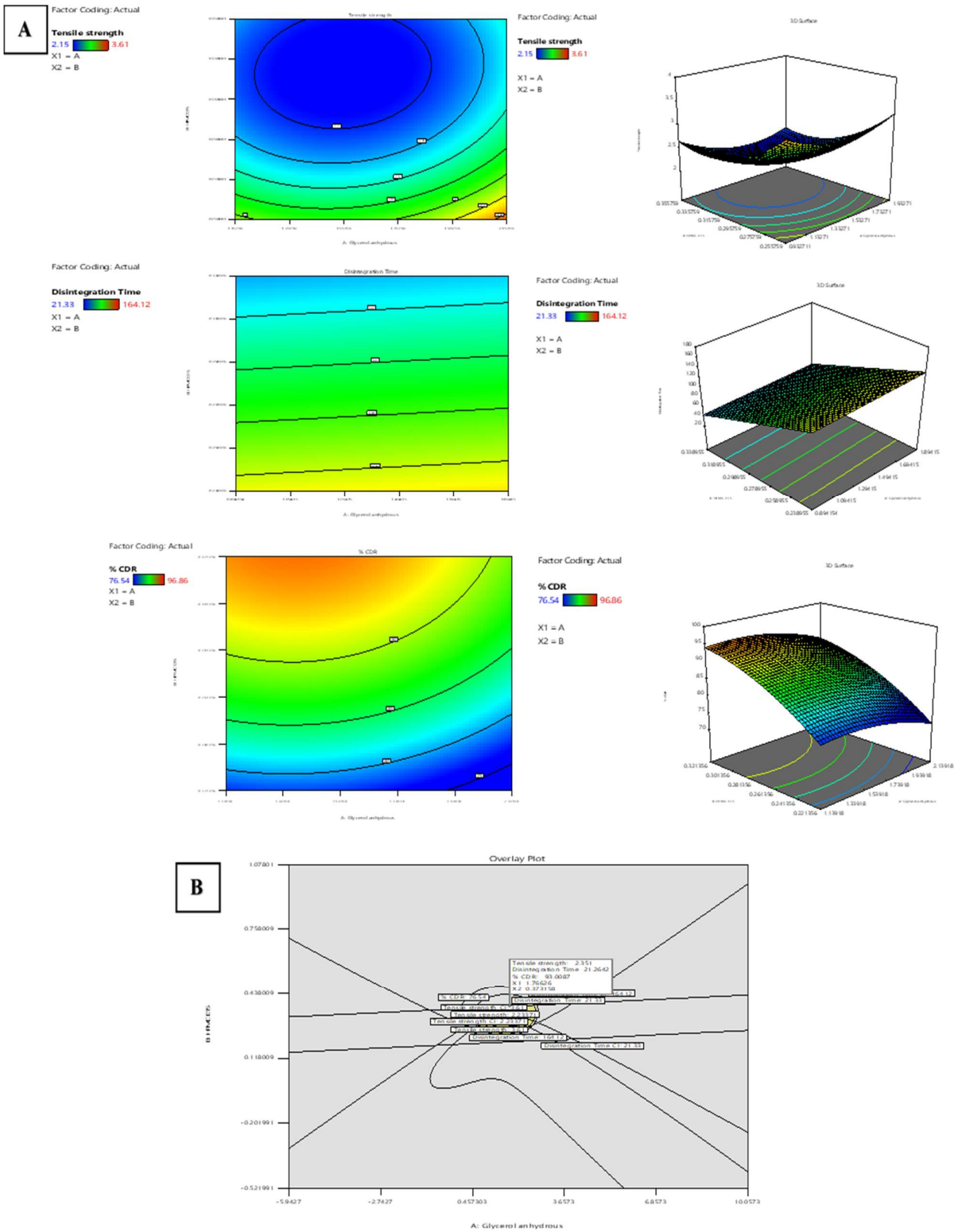
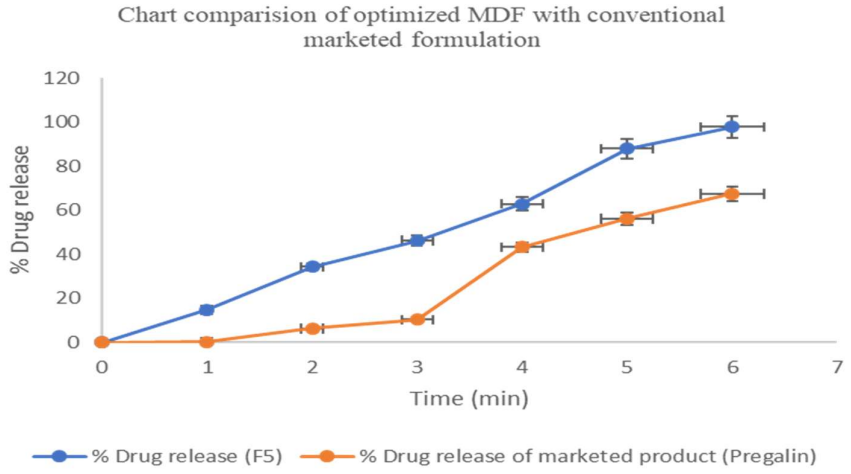
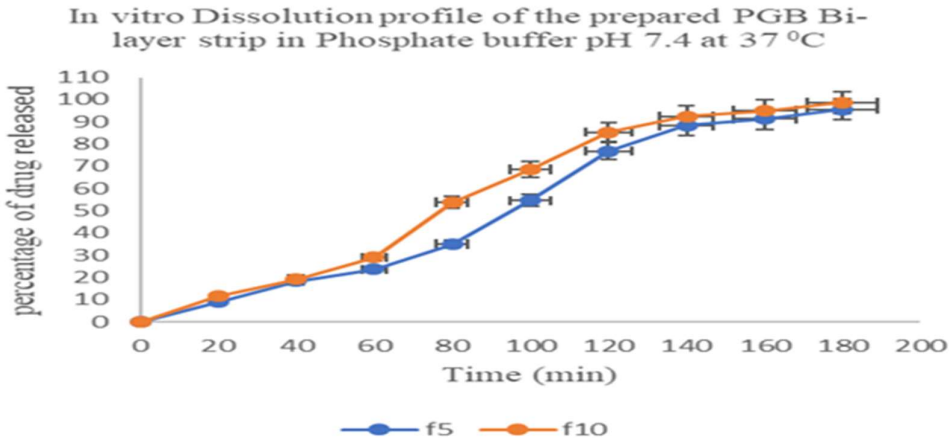


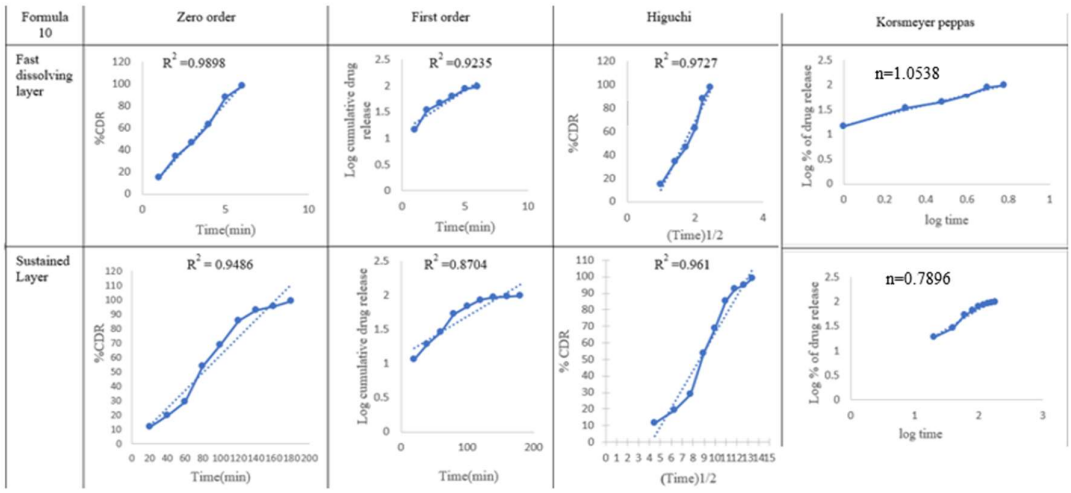
Figure 1: (A) Influence of independent variables on responses: The data presented were generated using software, and the surface plots and response surface plots were created using a factorial design. The figure illustrates the surface plot showing the impact of the variables on responses Y1, Y2, and Y3, as well as the response surface plot depicting the effect of the variables on these responses. (B) Overlay plot for optimized batch: Based on the attractiveness study and overlay analysis, the optimized batch was determined to include 1.76 ml of glycerol anhydrous plasticizer and 0.373 g of HPMC E15 polymer



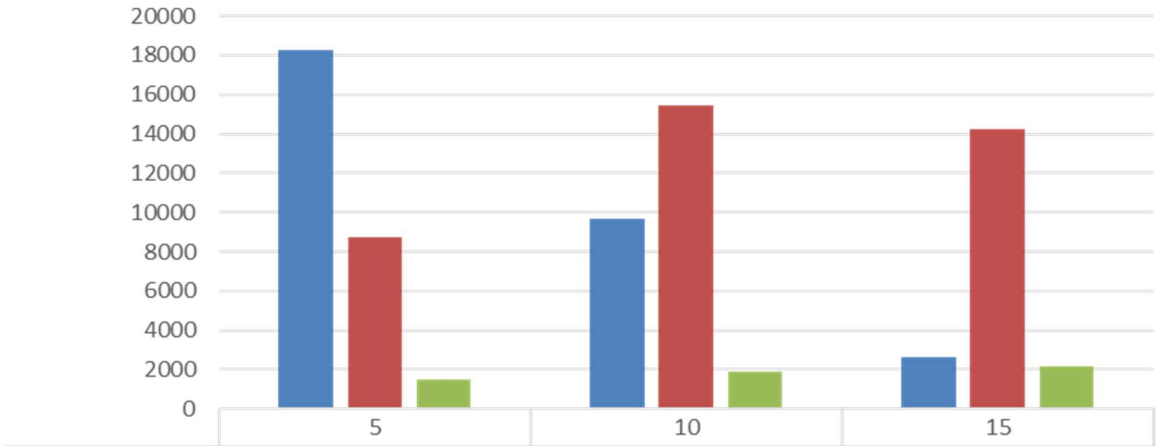
***All results are shown in mean ± S.D. (n=3)**
Figure 2: Chart comparison of optimized MDF with conventional marketed formulation



***All results are shown in mean ± S.D. (n=3)**
Figure 3: In vitro Dissolution profile of Pregabalin (PGB) bilayer strip in pH 7.4 Phosphate buffer at 37



***All results are shown in mean ± S.D. (n=3)**
Figure 4: Release kinetics analysis and mechanism of Pregabalin bilayer film



	5	10	15
API	18271	9652	2624
Test Formulation	8754	15475	14248
Marketed	1462	1874	2146

Figure 5: Depicted the in vivo drug release study plasma drug concentration over time (Minutes) comparing API, Test sample and Marketed formulation (Gabawin-50)

CONCLUSION:

This study aimed to develop a 50mg Pregabalin bilayer oral dissolving film, with 25mg in each layer (fast release and sustained release), improving their release profiles. Formula F5, consisting of a fast release layer with 1.5 ml glycerol anhydrous, 0.30 gm HPMC E15, and 0.075 gm Sodium starch glycolate, and a sustained release layer with Ethyl cellulose was chosen as the optimized formula. It showed a low disintegration time of 32 seconds, with 50% drug release in 80 minutes and sustained release over 180 minutes. The pharmacokinetic analysis of the buccal mucosal film demonstrated superior performance compared to the marketed tablet. This film circumvents first-pass metabolism, making it an effective formulation. As the drug is used for treating epilepsy in children, the buccal film improves patient compliance. Moreover, since the drug is ionized at gastric pH, the buccal route offers better absorption.

Ethical Committee: Male Inbred Wistar rats were used in the study, approved by the CPCSEA Ethical Committee (DL/IAEC/DIPS/09/2024/87). The study was conducted at Deshpande Laboratories Pvt. Ltd., an ISO 9001:2008 certified drug testing laboratory.

Applied for Patent

We have applied this formulation for patent in the PATENT OFFICE, Government of India with docket number 79963.

Funding source

None.

Conflict of Interest

None.

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REFERENCES

[1] Dey P, Ghosh A. Wafers: An Innovative Advancement Of Oro-Dispersible Films. International Journal Of Applied Pharmaceutics [Internet]. 2016 Jan 6;8(1):1–7. Available From: https://Journals.Innovareacademics.In/Index.Php/Ijap/Article/View/10531

[2] Mishra S, Kumar G, Kothiyal P. The Pharma Innovation Formulation And Evaluation Of Buccal Patches Of Simvastatin By Using Different Polymers. 2012;1(7). Available From: Www.Thepharmajournal.Com

[3] Gupta A, Kumar J, Verma S, Singh H. Application Of Quality By Design Approach For The Optimization Of Orodispersible Film Formulation. Asian Journal Of Pharmaceutical And Clinical Research. 2018;11(Special Issue 2):8–11.

[4] Joshi A, Kumar G. Fast Dissolving Thin Strips: An Emerging Way For Oral Drug Delivery, Indo Am. J P Sci [Internet]. 2018;(01):429–38. Available From: Http://Doi.Org/10.5281/Zenodo.1160888

[5] Mahmod Ws, Khalil Yi. Formulatio And Evaluation Of Zolmitriptan Bilayer Oral Strip [Internet]. Vol. 4, Wissam Et Al. World Journal Of Pharmaceutical Research. 2015. Available From: Www.Wjpr.Net

[6] Ketul P, Patel Kr, Patel Mr, Patel Nm. Fast Dissolving Films: A Novel Approach To Oral Drug Delivery. Vol. 4, International Journal Of Pharmacy Teaching & Practices. 2013.

[7] Patel Ar, Prajapati Ds, Raval Ja. Review Paper Fast Dissolving Films (Fdfs) As A Newer Venture In Fast Dissolving Dosage Forms [Internet]. Vol. 2, Int.J.Drug Dev. & Res. Available From: Http://Www.Ijddr.Com

[8] Arya A, Chandra A, Sharma V, Pathak K. Fast Dissolving Oral Films: An Innovative Drug Delivery System And Dosage Form. Vol. 2, International Journal Of Chemtech Research Coden.

[9] Mikaeloff Y, De Saint-Martin A, Mancini J, Peudenier S, Pedespan Jm, Vallée L, Et Al. Topiramate: Efficacy And Tolerability In Children According To Epilepsy

Syndromes. Epilepsy Res. 2003 Mar 1;53(3):225–32.

[10] Ouda Gi, Dahmash Ez, Alyami H, Iyire A. A Novel Technique To Improve Drug Loading Capacity Of Fast/Extended Release Orally Dissolving Films With Potential For Paediatric And Geriatric Drug Delivery. Aaps Pharmscitech. 2020 May 1;21(4).

[11] Dahmash Ez, Iyire A, Alyami Hs. Development Of Orally Dissolving Films For Pediatric-Centric Administration Of Anti-Epileptic Drug Topiramate – A Design Of Experiments (Doe) Study. Saudi Pharmaceutical Journal. 2021 Jul 1;29(7):635–47.

[12] Prajapati Bg, Patel P, Patel D. Mouth Dissolving Film As A Potential Dosage Form For Paediatric Usage. Journal Of Pharmaceutical And Biological Sciences. 2024 Feb 28;11(2):133–41.

[13] Winarti L, Laily Az, Sari Lork, Irawan Ed, Nurrahmanto D, Rosyidi Va, Et Al. Formula Optimization And In Vitro Release Kinetic Studies Of Diltiazem Hydrochloride Mucoadhesive Bilayer Buccal Film. International Journal Of Applied Pharmaceutics. 2021;13(Special Issue 2):7–12.

[14] Alves Tfr, Rios Ac, Pontes K Da S, Portella Dl, Aranha N, Severino P, Et Al. Bilayer Mucoadhesive Buccal Film For Mucosal Ulcers Treatment: Development, Characterization, And Single Study Case. Pharmaceutics. 2020 Jul 1;12(7):1–24.

[15] Kilor V, Sapkal N, Daud A, Humne S, Gupta T. Development Of Stable Nanosuspension Loaded Oral Films Of Glimepiride With Improved Bioavailability. International Journal Of Applied Pharmaceutics. 2017;9(2):28–33.

[16] Sadeq Za, Rajab Na. Studying The Effect Of Different Variables On The Formulation Of Mucoadhesive Buccal Patches Of Captopril. International Journal Of Applied Pharmaceutics. 2017;9(2):16–21.

[17] Li W, He W, Gao P, Zhang C, Cai H, Chen Y, Et Al. Preparation, In Vitro And In Vivo Evaluations Of Compound Calculus Bovis Sativus And Ornidazole Film. Vol. 39, Biol. Pharm. Bull. 1588.

[18] Patel A. Mucoadhesive Buccal Films Based On Chitosan And Carboxymethylated Feronia Limonia Fruit Pulp Mucilage Interpolymer Complex For Delivery Of Opioid Analgesics. Asian J Pharm. 2016 Jul;10:137.

[19] Patil Ps. Formulation And Evaluation Of Fast Mouth Dissolving Film Of Metoprlol Succinate. World J Pharm Pharm Sci. 2017 Jul 1;657–69.

[20] Vadodariya J, Chotaliya M. Development Of Bilayer Fast Dissolving Film Of Lidocaine Hcl And Choline Salicylate To Treat Localised Moderate To Severe Oral Pain [Internet]. Vol. 4, International Journal Of Research Publication And Reviews Journal Homepage: Www.Ijrpr.Com. 2023. Available From: Www.Ijrpr.Com

[21] Vergote Gj, Vervaet C, Remon Jp, Haemers T, Verpoort F. N Ear-Infrared Ft-Raman Spectroscopy As A Rapid Analytical Tool For The Determination Of Diltiazem Hydrochloride In Tablets [Internet]. Vol. 16, European Journal Of Pharmaceutical Sciences. 2002. Available From: Www.Elsevier.Nl/Locate/Ejps

[22] Patel Dm, Patel Dj, Darji Pj. Formulation And Evaluation Of Fast-Dissolving Film Of Cetirizine And Dextromethorphan. International Journal Of Pharmaceutical Sciences And Nanotechnology. 1970 Jan 1;9(3):3305–11.

[23] Preis M, Woertz C, Schneider K, Kukawka J, Broscheit J, Roewer N, Et Al. Design And Evaluation Of Bilayered Buccal Film Preparations For Local Administration Of Lidocaine Hydrochloride. European Journal Of Pharmaceutics And Biopharmaceutics. 2014;86(3):552–61.

[24] Tapre Dn, Borikar Sp, Jain Sp, Walde Sr, Tapadiya Gg, Gurumukhi Vc. Development And Evaluation Of Novel Famotidine-Loaded Fast Dissolving Sublingual Film Using The Quality-By-Design Approach. J Drug Deliv Sci Technol. 2023 Aug 1;85.

[25] Thabet Y, Breitkreutz J. Orodispersible Films: Product Transfer From Lab-Scale To Continuous Manufacturing. Int J Pharm. 2018 Jan 15;535(1–2):285–92.

[26] Thabet Y, Lunter D, Breitkreutz J. Continuous Inkjet Printing Of Enalapril Maleate Onto Orodispersible Film Formulations. Int J Pharm. 2018 Jul 30;546(1–2):180–7.

[27] Shafi H, Rashid R, Rather S Ullah, Siva Reddy D V., Azmi L, Abdal-Hay A, Et Al. Super Disintegrating Oromucosal Nanofiber Patch Of

Zolmitriptan For Rapid Delivery And Efficient Brain Targeting. Chemical Engineering Journal. 2023 May 1;463.

[28] Bassam M. Tashtoush Zsa, Najib Nm. In Vitro And In Vivo Evaluation Of Glibenclamide In Solid Dispersion Systems. Drug Dev Ind Pharm [Internet]. 2004;30(6):601–7. Available From: https://Doi.Org/10.1081/Ddc-120037491

[29] Prabhu P, Malli R, Koland M, Vijaynarayana K, D'Souza U, Harish N, Et Al. Formulation And Evaluation Of Fast Dissolving Films Of Levocitirizine Di Hydrochloride. Int J Pharm Investig. 2011;1(2):99.

[30] Mohamed Ms, El-Shenawy Aa, Hakim Ramadan A El, Mahmoud Ea, Amin Ma, Mohammed Ha, Et Al. Metolazone Co-Crystals-Loaded Oral Fast Dissolving Films: Design, Optimization, And In Vivo Evaluation. J Drug Deliv Sci Technol [Internet]. 2023;90:105167. Available From: Https://Www.Sciencedirect.Com/Science/Article/Pii/S1773224723010195

[31] Pol S V, Takarkhede S. Formulation And Evaluation Of Fast Dissolving Buccal Film Containing Vildagliptin [Internet]. American Journal Of Pharmacy & Health Research. 2018. Available From: www.Ajphr.Com

[32] Miller L, Orihuela C, Fronek R, Murphy J. Preparative Chromatographic Resolution Of Enantiomers Using Polar Organic Solvents With Polysaccharide Chiral Stationary Phases. J Chromatogr A [Internet]. 1999;865(1):211–26. Available From: https://Www.Sciencedirect.Com/Science/Article/Pii/S0021967399007438

[33] Karthik Kumar B, Thiruvengada Rajan Vs, Tanveer Begum N. Analytical Method Development And Validation Of Lidocaine In Ointment Formulation By U.V Spectrophotometric Method.

[34] Patil Kr, Surawase Rk, Pagare Sb, Vadje Ss, Shinde Me, Pawar Jd. A Review On Sustained Release Drug Delivery System. World Journal Of Pharmaceutical Research Www.Wjpr.Net [Internet]. 2020;9:390. Available From: Www.Wjpr.Net

[35] Mahmod Ws, Khalil Yi. Formulation And Evaluation Of Zolmitriptan Bilayer Oral Strip.

World J Pharm Res. 2015;4(1):25–57.

[36] Mishra S, Kumar G, Kothiyal P. The Pharma Innovation Formulation And Evaluation Of Buccal Patches Of Simvastatin By Using Different Polymers. 2012;1(7). Available From: www.Thepharmajournal.Com

[37] Shafi H, Rashid R, Rather S Ullah, Siva Reddy D V, Azmi L, Abdal-Hay A, Et Al. Super Disintegrating Oromucosal Nanofiber Patch Of Zolmitriptan For Rapid Delivery And Efficient Brain Targeting. Chemical Engineering Journal [Internet]. 2023; 463: 142481. https://Www.Sciencedirect.Com/Science/Article/Pii/S1385894723012123

[38] Thakur V, Dogra S, Verma S, Vashist H. Solubility Enhancement Techniques. World Journal Of Pharmaceutical Research www.wjpr.net | [Internet]. 2020;9. Available From: Www.Wjpr.Net

[39] Dixit Gr, Chavhan JI, Upadhye KP, Misra S. Formulation And Characterization Of Mucoadhesive Buccal Film Of Ranitidine Hydrochloride Using Sterculia Foetida Gum As Polymer. 2015;8.

[40] Peddapalli H, Chinnala Km, Banala N. Design And In Vitro Characterization Of Mucoadhesive Buccal Patches Of Duloxetine Hydrochloride. Int J Pharm Pharm Sci. 2017 Feb 1;9(2):52.