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DEVELOPMENT OF FORMULATION OF PERAMPANEL AS MOUTH DISSOLVING STRIPS AND IT'S EVALUATION

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ABSTRACT

The current study was carried out to develop a Perampanel mouth dissolving strip (MDS). Perampanel was used in individuals over the age of 12 to treat partial-onset seizures that may or may not be associated with generalised seizures. The medication was delivered to the place of application via oral mucosal tissues by the film. Because they are unable to consume tablets, this dose form is useful for comatose patients and people suffering from epilepsy. In this investigation, many film formulations with the medicine were created using various polymers and plasticizers to pick the best one with the optimal and needed properties. The film was created using the solvent casting process. The MDS was optimised using a full factorial design. The concentration of film former (HPMC-E15) and plasticizer were independent variables in this study (PEG-400). The response for this design was chosen based on disintegration time, folding endurance, and percent drug release after 5 minutes. All nine formulations (F1-F9) were characterised for various parameters and yielded excellent results. According to the results, the F7 batch has a disintegration time of 14.549 seconds, a density of 2822.039, and a percentage of 95.550.204 at 5 minutes.
KEYWORDS: Perampanel, Mouth dissolving strip, Buccal film, Antiepileptic

INTRODUCTION

Because it is the most convenient, cost-effective, and simple to give, the oral route is recommended, resulting in excellent patient compliance (approximately 90 percent of drugs administered via the oral route). In various locations, the keratinized and non-keratinized epithelium lining of the oral cavity vary in kind and thickness. Because a geriatric or paediatric patient who is frightened of choking may have difficulties swallowing, the oral route is preferable. Patient convenience and compliance-oriented research have resulted in safer and newer medication administration methods. Fast-dissolving systems have lately grown in popularity, giving consumers more options. This is because they offer quick disintegration or breakdown, as well as self-administration without the need for water or chewing. Both patients and doctors agree that the oral route is the best and most commonly utilised. The tablet is either formed of highly porous or soft-mold matrices, or it is crushed with very little force, making it friable and fragile and difficult to handle. A scientist at Wyeth laboratories in the United Kingdom developed the fast-dissolving films as an alternative to typical dosage forms in the late 1970s. This is an alternative to pills and capsules for both children and adults. Buccal medication administration has lately gained popularity. The most advanced oral dose form is oral strips, also known as oral films, oral dispersive films, and mouth dissolving films. It offers benefits over no-sugar-added strips, as opposed to syrups and certain tablets. It also had fewer calories than other pharmaceutical and supplement dose forms; some of the strips are lactose-free and gluten-free; and it was very convenient to carry; we could pack them in a tiny purse or pocket. On the oral dissolving strips, the dose form is exact. It improves efficiency by dissolving in the oral cavity in minutes. Because of the increased blood flow and permeability of the oral mucosa (4-1000 times larger), The mucosa has various advantages since it is adequately supplied with both vascular and lymphatic drainage. Furthermore, the first-pass metabolism of the hepatic liver and pre-systemic disposal of the gastrointestinal tract (GIT) are avoided. It is also

a low-cost choice in contrast to other medicines. Oral strips were created using hydrophilic polymers. Oral strips became popular after the launch and widespread usage of Listerine pocket strips in the early 2000s.

DRAWBACK OF CONVERSATION DOSAGE FORM

- Drug handling with wet hands and improper drug storage can cause chemical degradation due to humility and temperature.
- Patient's incompliance was high
- Bioavailability problem noted
- Drug taking longer time to be absorbed compared to mouth dissolving strips
- Liquid oral dosage has a stability problem
- Drug has an unpleasant taste
- If patients were unconscious or with a locked-jaw condition it will be difficult to shallow
- Patients with mental illnesses who refuse to take medication
- Patients with cancers of the mouth or throat

IDEAL CHARACTERISTICS OF MOUTH DISSOLVING ORAL FILMS

- Drug administration without water
- Cost-effective method was used
- Leave no or minimal amounts of residue in the mouth
- Avoid first-pass metabolism phase
- Avoid gastric intestinal irritation (GIT)
- It should be able to produce the rapid effect
- It requires good taste
- The drug should be moisture resistant and easily soluble in saliva
- Ionized in the oral cavity
- Easily penetrate the Oral Mucosa

MERITS OF MOUTH DISSOLVING STRIPS

- Easy to used
- No need for water
- Travel friendly, More flexible, Easily handle storage
- Don't produce any type of suffocation condition
- Maximum stability
- Less or no residue in the mouth left
- The gastrointestinal tracks were bypassed and bioavailability increased to maximum
- Dosage was low and produced very few side effects
- Patients who suffer from nausea or who those receiving any kind of chemotherapy
- Easy to administration to unconscious patients or locked-jaw condition
- It provided more accurate dosage when compared to liquid dosage form
- Left good taste in the mouth
- Provided onset action, the drug goes directly into blood circulation which affects a condition requiring urgent intervention
- Drug was absorbed maximum no wasted, improve dosing accuracy
- Those drugs that have less bioavailability or fewer water-soluble drugs, It enhanced
- Doesn't prevent normal function like drinking or speaking
- The administration of the drug with a high risk of disruption in GIT.
- It has expanded market and provide a variety
- Is cost-effective compare to ordinary tablets and capsule
- Easy manufacturing methods

DEMERITS OF MOUTH DISSOLVING STRIPS

- Require special packing
- Not suitable for drugs that irritate the oral pH
- Limited dose of medication can administration
- Produced long team difficulties
- The only drugs absorbed by passive diffusion can be applied in this way
- Dose termination is not possible
- Not registered to any pharmacopeia
- The method of preparation is costly compared to oral dissolving tablets

MATERIALS AND METHODS

MATERIALS: Perampanel was provided as a free sample by the Torrent Research Center in Gandhinagar, Gujarat, India. Colorcon Goa supplied the hydroxy methylcellulose HPMC- E15, while Mohini Chemical in Mumbai supplied the PEG 400. Corel Pharma Ahmedabad provided a free sample of Kyron T314. Signet Chemicals Ltd., Mumbai, provided the citric acid and mannitol. The remaining reagents were of analytical grade.

IDENTIFICATION OF DRUG

The DSC thermogram of Perampanel sample was recorded by heating the sample at constant rate 10 ˚c -200˚c using DSC apparatus Perkin Elmer, USA. Differential Scanning Calorimetry (DSC) Thermogram of sample was recorded by heating the sample at constant rate 10^{o}C /min in temperature range 50^{0}c– 230^{0}c using DSC apparatus ((Perkin Elmer, USA

Preparation of mouth dissolving strip

Perampanel buccal films were made using the solvent casting process, which is the most extensively utilised method for making MDS. Water-soluble components are created by mixing them together in a heated magnetic stirrer. The combination is then treated with medications and other excipients to create a viscous solution**.**

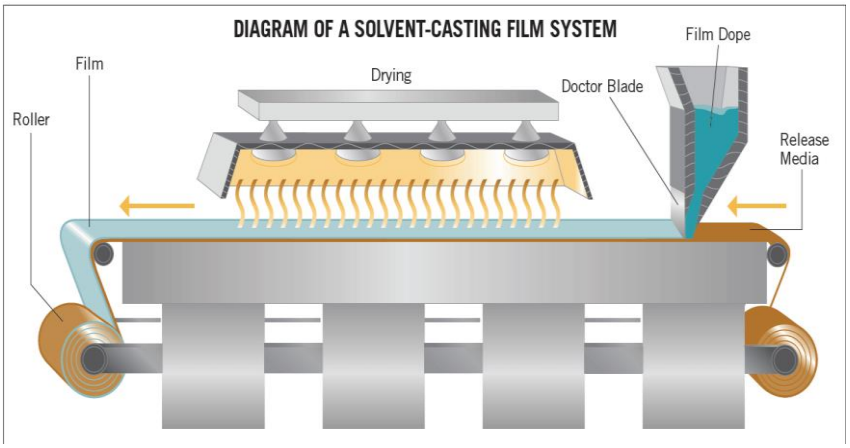


Figure ***Error! Use the Home tab to apply 0 to the text that you want to appear here.****..1 diagram of solvent casting film*

Pouring the solution into a petri dish and letting the solvent to evaporate is the procedure used here. These are maintained at room temperature for 20-25 or 24-48 hours depending on the solvent system employed, or for a shorter duration at 40°C-50°C in the oven. The films are 15-20 mm in diameter and 0.2-0.3 mm thick once the solvents have evaporated, and they must be carefully detached from the Petri plates. They are sliced into the required size pieces based on the amount of active ingredient present. The semisolid state gel mass is poured into suitable moulds and dried with gel-forming polymers in the semisolid technique. After that, they are cut into the desired sizes. Showed in fig.

Table 1 Formulation component of MDS

Polymers	**Category**	**Amount**
HPMC- E15,	Film former polymer	40-50%
Polyvinyl glycol- 400	Plasticizer	0-20%
Mannitol	Sweeting agent	3-6%
Citric acid	Flavouring agent	q. s
Kyron	Super disintegrants	0-8%

Table 2 formulation batches

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Perampanel	19.23	19.23	19.23	19.23	19.23	19.23	19.23	19.23	19.23
HPMC E15	600	525	750	750	750	600	525	600	525
Propylene glycol	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
Kyron	140	40	140	40	90	40	140	140	90
Citric acid	30	30	30	30	30	30	30	30	30
Mannitol	25	25	25	25	25	25	25	20	20
Distilled water (ml)	15	15	15	15	15	15	15	15	15

Weight variation

It can be calculated by individually weighing same size of strip (20mm x 20mm). 10 strips must be taken for weight variation test. Average weight standard deviation is calculated for each batch. Weight variation should be in the rangeof ± 5%.

Thickness

Because strip thickness is directly connected to drug content consistency, it must be monitored. Calibrated Vernier callipers and a digital micrometre can be used to measure it. The thickness of the strip is measured at five separate sites, and the average of these five spots is used to calculate the thickness of the strip. The thickness variation should be less than 5%. For thickness consistency, at least 5 strips must be taken.

Surface pH

Take a 20mm-by-20mm piece of film. A suitable amount of water is used to dissolve the strip. The pH of a solution is determined by placing the electrode of a pH metre in contact with it and allowing it to stabilise. Repeat this method three times to obtain the average pH value. Consider this average to be the pH of the film.

% Drug content

Take a 20mm-by-20mm piece of film and dissolve it in 100 cc of clean water, shaking well. Filter the liquid. Using a UV spectrophotometer, measure the absorption. Repeat this method three times to obtain the average absorbance value. This average figure is entered into the algorithm to determine the drug content of the film, which should be in the 5% range.

Flexibility (folding endurance)

Thin strip' flexibility is determined by folding them at an angle of 180° in the same place until they break. Before breaking, the number of folds made is recorded. Excellent flexibility is defined as a film with a folding endurance of 250 times or more.

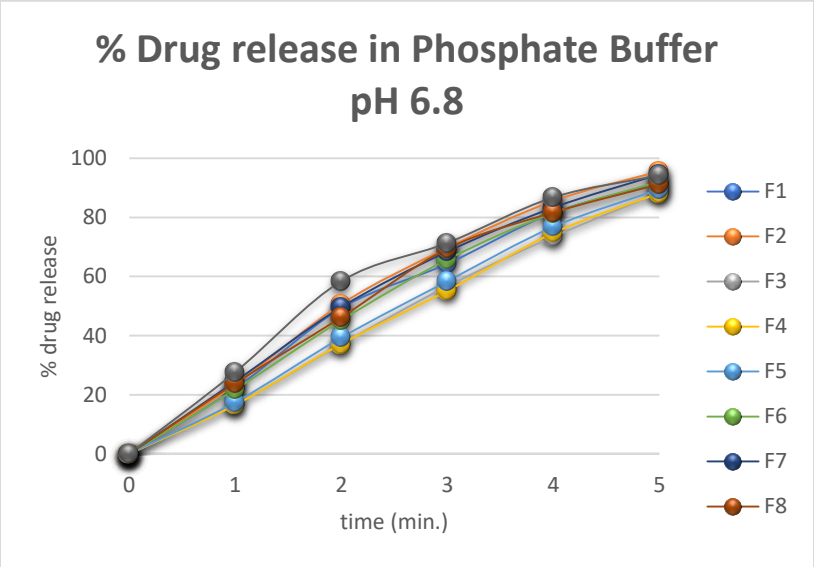
Disintegration test

There are no official criteria for the mouth dissolving strip. Take a 20mm by 20mm piece of film. According to the CDER guidelines, the disintegration time of a film should be less than 30 seconds or less than the disintegration time of an orally disintegrating tablet. Fill a petri plate with 10 mL of filtered water or simulated salivary fluid. The strip is then placed in a Petri dish, and the time it takes for the film to degrade is recorded as the disintegration time.

IN-VITRO Dissolution

The produced film's dissolution profile is measured using a USP type II instrument (Paddle apparatus). The dissolve media for the oral dissolving strip is 500 cc Phosphate buffer pH 6.8. The dissolving rate of sublingual film is 50 RPM. Maintain the temperature of the dissolving medium at 37 ºC + 0.5 ºC. The sample collecting interval is 1 minute. To maintain the desired volume of dissolving media, new medium is introduced following the sample collection. The absorbance of collected samples is measured at 340 nm using a UV spectrophotometer. The calibration curve is used to calculate the percentage of drug release. The graph depicts the percentage of medication released vs time.

Figure ***Error! Use the Home tab to apply 0 to the text that you want to appear here.****.2 % Drug release*



Time (min)	% Cumulative Drug Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	**0**	0	0	0	0	0
1	22.12± 0.37	23.45± 0.69	16.65± 0.41	16.5± 0.70	17.45± 0.75	21.78± 0.21	24.49± 0.15	23.87± 0.45	27.65± 0.64
2	49.31± 0.62	50.65± 0.51	37.12± 0.59	37.24± 0.78	39.34± 0.35	45.22± 0.45	49.63± 0.65	46.23± 0.24	58.44± 0.54
3	64.32± 0.89	69.65± 0.41	56.71± 0.30	55.23± 0.38	58.43± 0.24	65.78± 0.75	68.45± 0.80	69.46± 0.36	71.36± 0.44
4	81.56± 0.19	85.56± 0.33	73.51± 0.88	74.78± 0.40	76.87± 0.25	81.54± 0.64	83.35± 0.45	81.72± 0.21	86.78± 0.51
5	91.46± 0.21	94.64± 0.28	88.35± 0.32	88.27± 0.29	89.57± 0.71	92.14± 0.19	95.55± 0.20	91.3± 0.15	94.28± 0.24
Average ± Standard Deviation (n=3)									

***In-vitro* drug release of factorial batches**

When compared to other batches, formulations with a smaller quantity of film forming ingredient had a shorter disintegration period. Disintegration time rises with increasing concentration of film forming agent. It has been discovered that formulations with a lower concentration of plasticizer have a poorer folding durability. The folding endurance rises as the concentration of plasticizer increases. It can be seen that the concentration of plasticizer has an effect on the disintegration time. The formulation with a higher amount of plasticizer has a somewhat longer disintegration time with the same concentration of film forming agent. The surface pH of all batches is close to 7, which is acceptable. The weight variation and composition uniformity of all batches were determined to be within limits. According to the in-vitro drug release statistics, batch F7 had a maximum drug release of 95.55 percent at 5 minutes when compared to other batches. The disintegration time of batch F7 is the shortest (14 seconds), and the folding endurance (282) is within acceptable limits. As a result, it is considered that the F7 batch is by far the best batch.

Results and discussion

Drug Excipient Compatibility by DSC

DSC tested drug excipient compatibility. The drug's spectrum with various excipients is shown below. The DSC spectra of the drug and excipients revealed that all of the key excipients were present even when the excipients were mixed. As a result, there is no interaction between Perampanel and the other excipients. As a result, Perampanel is stated to be compatible with the excipients used in film formulation.

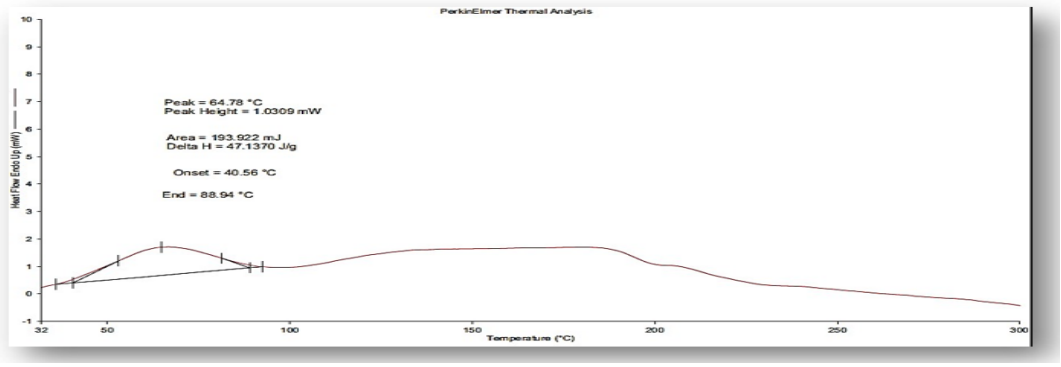


Figure1.3 DSC Graph of Mouth Dissolving Film of Perampanel

OPTIMIZATION OF MOUTH DISSOLVING STRIP OF PERAMPANEL USING 3^2 FULL FACTORIAL DESIGN

Table1.5 Evaluation of factorial batches

Parameters	F1	F2	F3	F4	F5
Size (mm)	20x20	20x20	20x20	20x20	20x20
Thickness (mm)	0.111 ± 0.002	0.103 ± 0.002	0.108 ± 0.003	0.113 ± 0.002	0.115 ± 0.002
Surface pH	6.8 ± 0.133	6.9 ± 0.098	6.9 ± 0.101	0.285 ±0.05	0.310±0.013
Weight variation (mg)	0.298 ± 0.035	0.310± 0.011	0.321 ± 0.014	7.0 ± 0.123	6.8 ± 0.101
% Drug content	98.3±0.32	98.9±0.17	99.2±0.21	98.7 ± 0.179	99 ± 0.093
Folding endurance	276± 1.414	250 ± 2.327	301 ± 2.244	293 ± 1.624	297 ± 2.039
Disintegration time (sec)	30± 0.489	22 ± 0.198	26 ± 1.010	35 ± 0.097	31 ± 0.748
% CDR at 5 min	91.46± 0.45	94.64± 0.24	88.35 ± 0.25	88.27 ± 0.18	89.57 ± 0.21
Average ± standard deviation (n=3)					

Table1.6 Evaluation of factorial batches

Parameters	F6	F7	F8	F9
Size (mm)	20x20	20x20	20x20	20x20
Thickness (mm)	0.117 ± 0.003	0.108 ± 0.002	0.118 ± 0.002	0.121 ± 0.003
Surface pH	0.325±0.009	6.9 ± 0.195	6.9 ± 0.248	6.9 ± 0.103
Weight variation (mg)	6.8 ± 0.132	0.300 ± 0.004	0.302 ± 0.018	0.294 ± 0.016
% Drug content	99.56 ± 0.80	99.24 ± 0.326	98.92 ± 0.074	99.3 ± 0.141
Folding endurance	270 ± 2.520	282 ± 2.039	260 ± 2.717	255 ± 3.120
Disintegration time (sec)	33 ± 1.019	14 ± 0.549	27 ± 0.982	19± 1.102
% CDR at 5 min	92.14 ± 0.30	95.55 ± 0.14	91.3 ± 0.25	94.28 ± 0.41
Average ± standard deviation (n=3)				

Generation of Quadratic Model for 32 Full Factorial Design

Table 1.7 Slection of variables

Independent Variables					
X_1			**X_2**		
Concentration of Film Forming Agent (HPMC E15) (mg)			**Concentration of Plasticizer (PEG- 400) (mg)**		
-1	**0**	**+1**	**-1**	**0**	**+1**
30	**40**	**50**	**1**	**4.5**	**8**
Dependent Variables					
Y_1		**Y_2**		**Y_3**	
Disintegration Time (sec)		**% drug release**		**Folding Endurance (No. of folds)**	

Formulation number	Coded Value		Actual Value	
	Concentration of Film Forming Agent (HPMC) (X_1)	Concentration of Plasticizer (PEG- 400) (X_2)	X_1 (%)	X_2 (%)
F1	-1	-1	30	1
F2	1	-1	50	8
F3	-1	1	30	1
F4	1	1	50	8
F5	-1	0	30	1
F6	1	0	50	8
F7	0	-1	40	4.5
F8	0	1	40	4.5
F9	0	0	40	4.5

Table 1.9 Quadratic model regression analysis for 3^2 full factorial design

Y1 – Disintegration Time (sec)	R1= 30.44+4.67*A-3.67*B+2.00*AB-5.67*A^2-0.6667*B^2
Y2 - % Drug Release (at 5 min)	R2= 90.99-0.8650*A+0.2300*B-2.10*AB
Y3 - Folding Endurance	R3= 276.00+21.00*A+5.00*B

Response Y1- Disintegration Time

To develop a quadratic equation for answer Y1, a polynomial regression analysis was performed (Disintegration time). According to the quadratic equation, the coefficients of HPMC E5 (X1) and PEG- 400 (X2) both have a substantial influence on Y1. A positive sign coefficient such as HPMC E15 implies that as the value of this variable grows, so does the disintegration time, and vice versa. PEG- 400 has a negative sign, which means that when the value of this variable grows, the disintegration time reduces and vice versa. A higher value of the coefficient HPMC E15 suggests that it has a greater impact on Y1 than the coefficient PEG- 400.

Response Y_2- % Drug Release

To develop a quadratic equation for answer Y2, a polynomial regression analysis was performed (percent Drug Release). According to the quadratic equation, the coefficients of both factors have a considerable influence on Y2. HPMC E15 has a negative sign, indicating that when the value of this variable grows, the percent drug release drops and vice versa. PEG-400 is a positive sign coefficient that implies that as the value of this variable grows, so does the percent drug release and vice versa. Response Y3- Folding Endurance

A polynomial regression analysis was done to generate quadratic equation for response Y_3 (Folding endurance). The quadratic equation indicate that coefficient of HPMC E15(X_1) and PEG- 400 (X_2) both have significant effect on Y_3. Both coefficient HPMC E15 and PEG-400 have positive sign indicates that as the value of this variables increases, the folding endurance increases and vice versa. Higher value of coefficient PEG- 400indicates that it has more significant effect on Y_3 than thecoefficient HPMC E15.

Statistical Analysis of Response Y1- Disintegration Time

Table 1.10 ANOVA for Quadratic model for response Y1

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	292.44	5	58.49	24.68	0.0122	significant
A-HPMC -E15	130.67	1	130.67	55.13	0.0051	
B-KYRON T-314	80.67	1	80.67	34.03	0.0100	
AB	16.00	1	16.00	6.75	0.0805	
A^2	64.22	1	64.22	27.09	0.0138	
B^2	0.8889	1	0.8889	0.3750	0.5836	
Residual	7.11	3	2.37			
Cor Total	299.56	8				

Factor coding is **Coded**.

Sum of squares is **Type III - Partial**

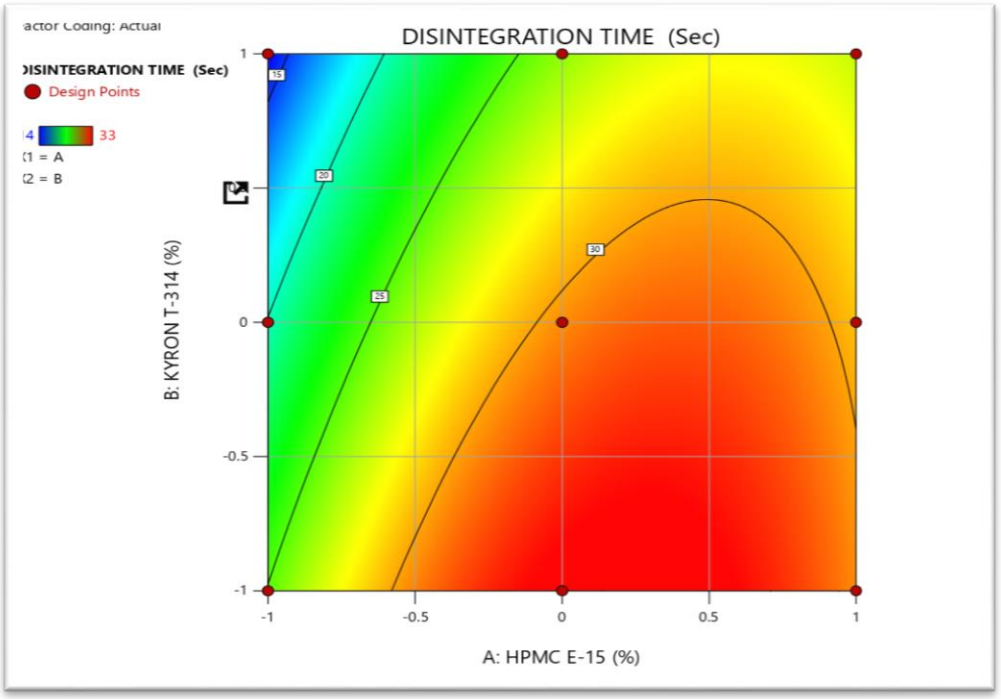
The **Model F-value** of 24.68 implies the model is significant. There is only a 1.22% chance that an F-value this large could occur due to noise.

P-values less than 0.0500 indicate model terms are significant. In this case A, B, A^2 are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

Quadratic Equation for Response Y_1

Y_1 - Disintegration time(sec)	R_1= 30.44+4.67*A-3.67*B+2.00*AB-5.67*A^2 -0.6667*B^2

The equation in terms of actual factors can be used to make predictions about the response for given levels of each factor. Here, the levels should be specified in the original units for each factor.It was observed that concentration of HPMC E15 is directly and Concentration of PEG- 400 is inversely proportional to the Y_1 - Disintegration time. So, when the value of HPMC E15 increases, the disintegration time



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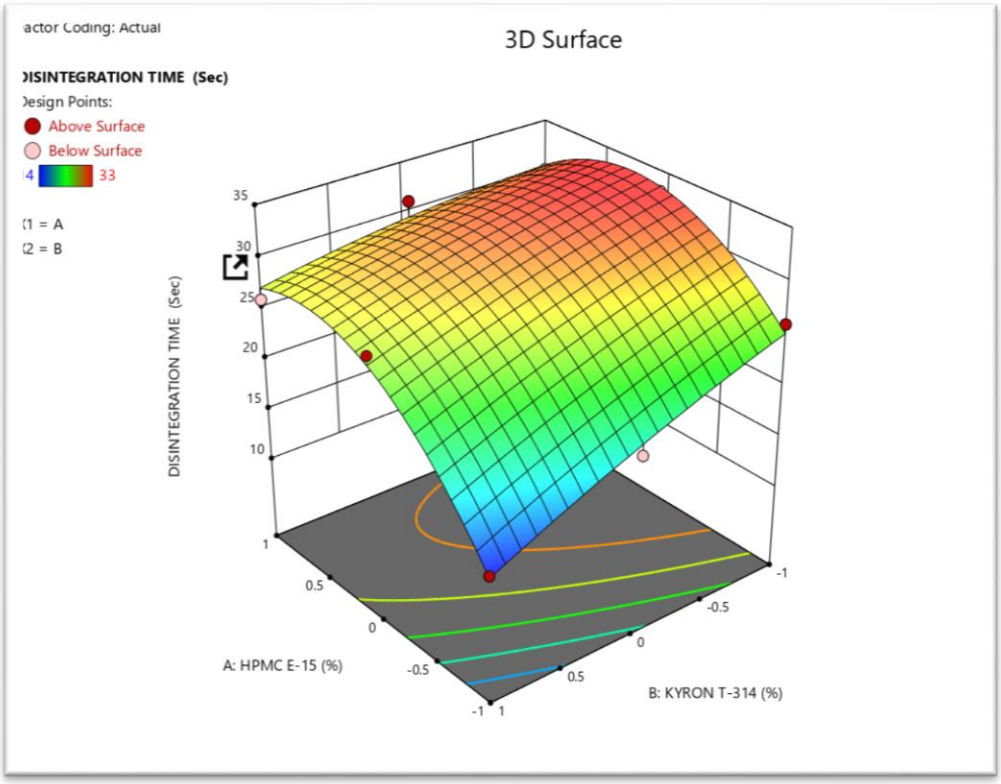

According to the 3-D surface counter plot and the contour plot, the concentration HPMC E15 (X1) has a greater influence on the response Y1 (Disintegration time) than the concentration PEG- 400. (X2). As observed in the contour plot, as the concentration of HPMC E15 grows, so does the disintegration time, and as the concentration of plasticizer increases, so does the disintegration time, therefore it is determined that the concentration of plasticizer should be in the medium range.

Positive sign of HPMC E15 and negative sign of PEG- 400 indicate the direct and inverse proportionality with response Y_1 respectively.

Statistical Analysis of Response Y2- % Drug Release

Response Y_2 was analyzed using Design Expert 13 software and the polynomial quadraticequation was generated.

Table 1.11 ANOVA for 2FI model for response Y_2

Source	**Sum of Squares**	**df**	**Mean Square**	**F-value**	**p-value**	
Model	22.45	3	7.48	7.56	0.0263	significant
A-HPMC E-15	4.49	1	4.49	4.54	0.0864	
B-KYRON T-314	0.3174	1	0.3174	0.3209	0.5956	
AB	17.64	1	17.64	17.83	0.0083	
Residual	4.95	5	0.9892			
Cor Total	27.39	8				

Factor coding is **Coded**.

Sum of squares is **Type III - Partial**

The **Model F-value** of 7.56 implies the model is significant. There is only a 2.63% chance that an F-value this large could occur due to noise.

P-values less than 0.0500 indicate model terms are significant. In this case AB is a significant model term. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

Quadratic Equation for Response Y_2

Y_2 - % Drug Release	R_2= 90.99-0.8650*A+0.2300*B-2.10*AB

The equation in terms of actual factors can be used to make predictions about the response for given levels of each factor. Here, the levels should be specified in the original units for each factor.

It was observed that concentration of HPMC E15 is inversely and Concentration of PEG- 400 is directly proportional to the Y_2 - % Drug release. So, when the value of HPMC E15 increases, the % drug release decreases and when the value of PEG- 400 increases, the % drug release increases.

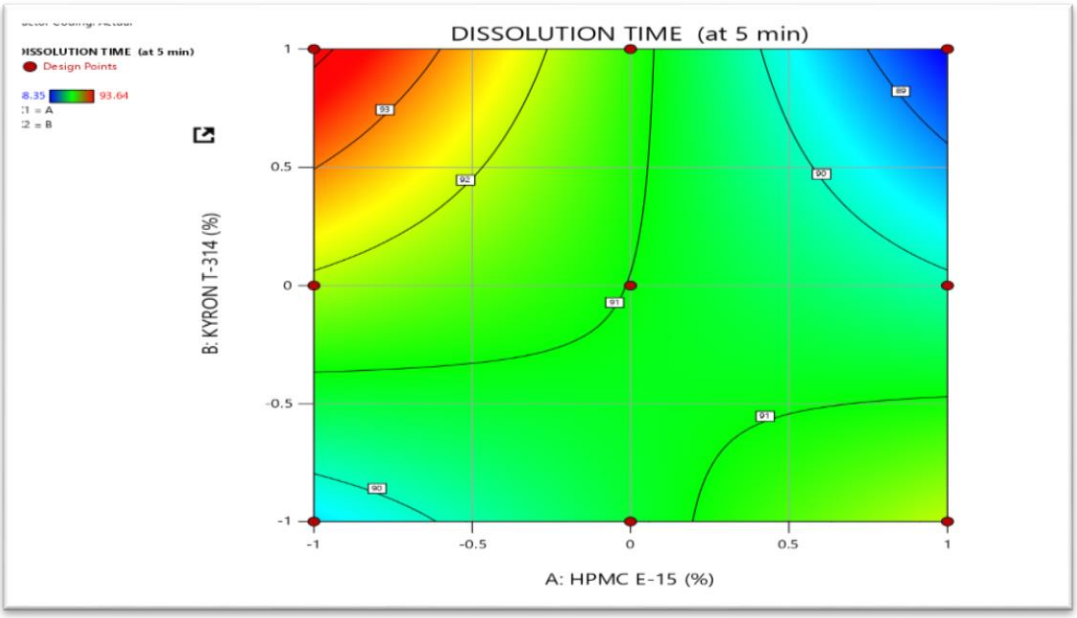

Figure 1.4 Contour plot of response Y2

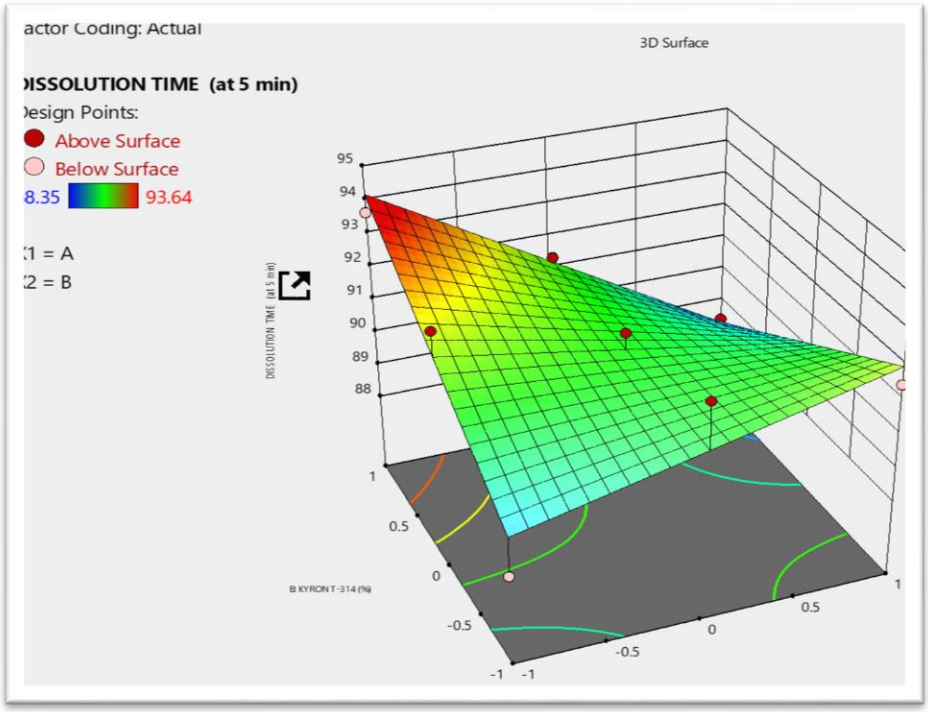

Figure 1.5 3-D Surface contour plot for response Y2

As observed from the 3-D surface counter plot and the contour plot, the effectiveness of concentration HPMC E15 (X_1) is more on the response Y_2 (%Drug release) than thatof concentration of PEG- 400 (X_2). As seen in contour plot concentration of HPMC E15 increases, % drug release decreases and concentration of plasticizer increases, % drug release increases but if concentration of plasticizer in higher level than % drug release decreases so it is concluded that concentration of plasticizer shouldbe in medium level.

Negative sign of HPMC E15 and positive sign of PEG- 400 indicate the inverseand direct proportionality with response Y_2 respectively.

Statistical Analysis of Response Y3- Folding Endurance

Response Y_3 was analyzed using Design Expert 13 software and the polynomial quadraticequation was generated.

Table 1.11 ANOVA for Linear model for response Y3

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	2796.00	2	1398.00	2097.00	< 0.0001	significant
A-HPMC E-15	2646.00	1	2646.00	3969.00	< 0.0001	
B-KYRON T-314	150.00	1	150.00	225.00	< 0.0001	
Residual	4.00	6	0.6667			
Cor Total	2800.00	8				

Factor coding is **Coded**.

Sum of squares is **Type III – Partial** The **Model F-value** of 2097.00 implies the model is significant. There is only a 0.01% chance that an F-value this large could occur due to noise. **P-values** less than 0.0500 indicate model terms are significant. In this case A, B are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

Quadratic Equation for Response Y_3

Table 0.2 Quadratic Equation for Response Y3

Y_3 - Folding endurance	R3= 276.00+21.00*A+5.00*B

The equation in terms of actual factors can be used to make predictions about the response for given levels of each factor. Here, the levels should be specified in the original units for each factor. It was observed that concentration of HPMC E15 and Concentration of PEG- 400 is directly proportional to the Y_3 - Folding endurance. So, when the value of HPMC E15 and PEG- 400increases, the folding endurance increases.

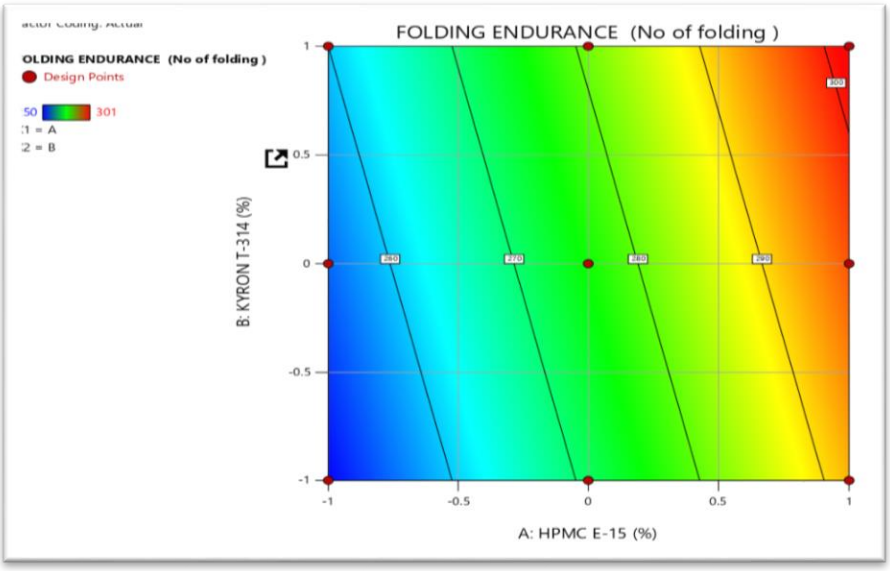

Figure 1.6 Contour plot of response Y3

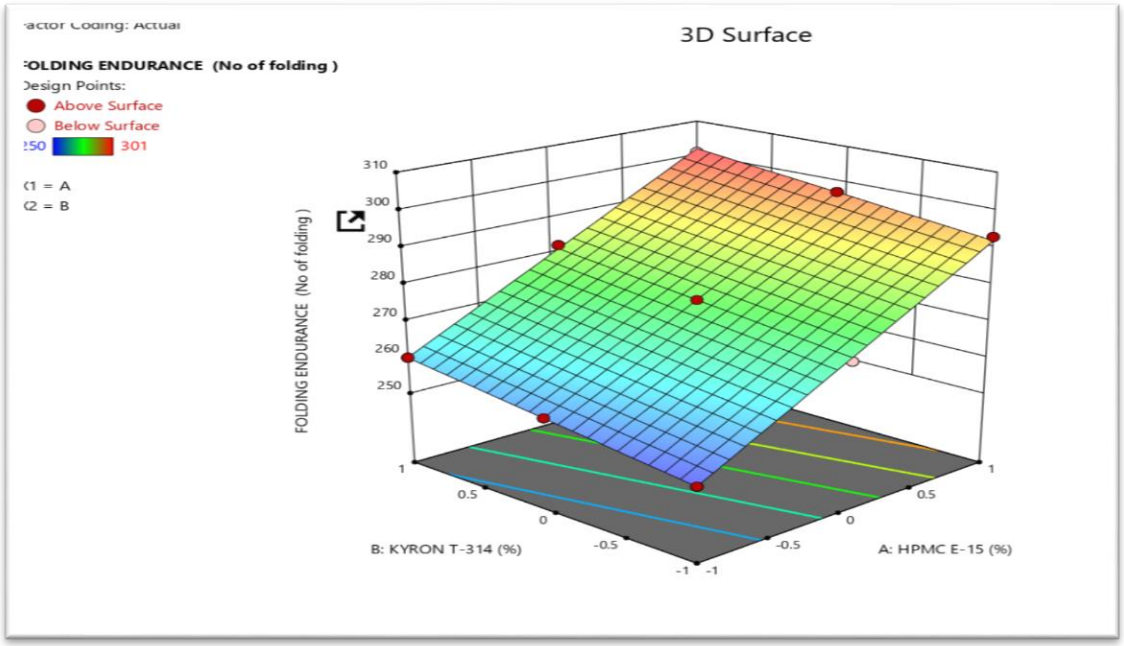

Figure ***Error! Use the Home tab to apply 0 to the text that you want to appear here.****1.7 D Surface contour plot of response Y3*

As observed from the 3-D surface counter plot and the contour plot, the effectiveness of concentration PEG- 400 (X_2) is more on the response Y_3 (Folding endurance)than that of concentration of HPMC E15 (X_1). As seen in contour plot concentration ofHPMC E15 and concentration of plasticizer increases, folding endurance increases. Positive sign of HPMC E15 and PEG- 400 indicate the direct proportionality with response Y_2.

Optimization of Formulation by Overlay Plot

The 3^2 Full Factorial Design was applied for the determination of the effects of independentvariables on the responses. In this study the effect of independent variables X_1 (concentration of HPMC E15) and X_2 (concentration of PEG- 400) were analyzed and the optimized batch was selected from the overlay plot of these variables with the dependent variables Y_1, Y_2 and Y_3.

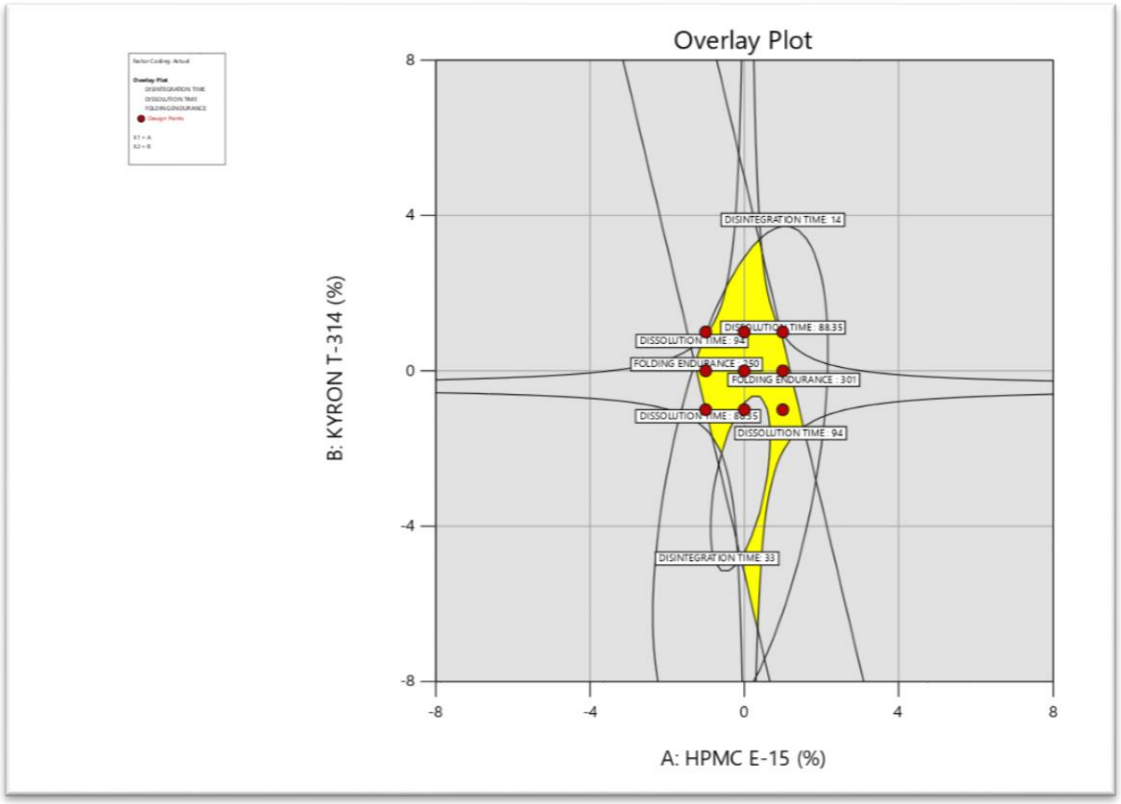

Figure 1.8 Overlay plot of responses with respect to independent variables

Optimized area was generated by Design Expert 13 using Overlay plot is given in the figure 6.21 any combinations of independent variables in the yellow region will give the desired results on dependent variables. Moreover, Response Y_1 (Disintegration time) was set in the range of, Response Y_2 (drug release) was set in therange of and Response Y_3 (folding endurance) was set in the range of.

Conclusion

The current study focuses on the development and testing of a Perampanel mouth dissolving strip. Perampanel, commonly known as an anti-epileptic medication, comes in a variety of forms. Perampanel, which is marketed in tablet form under the brand name Fycompa, is an anti-epileptic medication used to treat partial-onset seizures in persons over the age of twelve. Perampanel is now available in tablet and suspension formulations. Patient compliance with oral dose forms is poor. Because oral absorption is limited, it takes time for effect to occur. As a result, the current study was conducted on a Perampanel mouth dissolving strip formulation that promotes patient compliance as well as immediate medication action. The mouth dissolving strip is prepared by solvent casting method which is easy, require less time. Perampanel FTIR research and melting point measurement were performed to ensure its purity, and the results were good, indicating that the medicine is pure. Perampanel was spectrophotometrically analysed in water for the calibration curve. Preliminary batches were created using various film-forming agents and plasticizers to determine which excipients produced the greatest results in terms of disintegration time and folding durability. HPMC E15 was chosen as the film forming agent, while PEG-400 was chosen as the plasticizer, which also acts as a permeation enhancer. DSC was used to verify the drug excipient compatibility; there is no interaction, hence there is no drug excipient incompatibility. For 32 full factorial designs, two independent factors - film forming agent concentration (X1) and plasticizer concentration (X2) - were chosen, and nine batches F1-F9 were formulated and evaluated by three dependent responses - disintegration time (Y1), percent drug release (Y2), and folding endurance (Y3) (Y3). The batch F7 produced the greatest results, with disintegration taking only 14 seconds At 5 minutes, folding endurance was 282 1.624 and cumulative drug release was 95.55 0.20 percent. As a result, the F7 batch was designated as the optimised batch. Design Expert 13 was used to examine the effect of independent variables such as film forming agent concentration (HPMC E15) and plasticizer concentration (PEG-400) on the dependent variables such as disintegration time, percent drug release, and folding endurance in the formulation using a quadratic polynomial model.

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