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FORMULATION AND EVALUATION OF BUDESONIDE ORODISPERSIBLE FILM FOR EOSINOPHILIC ESOPHAGITIS

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Abstract: EOE is a long-term immune-mediated condition causing esophageal dysfunction and inflammation. Treatment options include proton pump inhibitors and swallowed topical steroids. This study aims to develop an orodispersible film containing budesonide, a poorly soluble anti-inflammatory medication, based on limited trials. The solvent casting technique is used to formulate orodispersible film. Preliminary batches were prepared for the selection of polymers, and from the preliminary batches, HPMC E15 LV combined with PEG 400 as a plasticizer demonstrated outstanding in vitro disintegration time and cumulative percent dissolution. A 32 factorial design with three levels and two factors was used, with polymer (X1) and plasticizer (X2) as independent variables. Formulated films were evaluated for their appearance, thickness, weight variation, surface pH, folding endurance, disintegration time, and in vitro dissolution rate. After evaluating the various batches of films, the F5 batch achieved the desired results, releasing 98.82% of the medication in just 5 minutes, resulting in quick film dissolution.

Keywords: *Eosinophilic Esophagitis (EOE), Budesonide, HPMC E15, Solvent casting, Orodispersible film (ODF).*

INTRODUCTION

EOE was defined as an esophageal disease characterised clinically by esophageal dysfunction symptoms and histologically by eosinophil-predominant histology. Eosinophilic esophagitis (EOE) is a newly recognised chronic inflammatory oesophageal disorder that affects both children and adults and is growing increasingly common worldwide.[1] Symptoms are similar to those of gastroesophageal reflux disease, however the diseases differ in histology, gene expression profile, drug responsiveness, hereditary risk, and association with allergens. EOE is difficult to identify clinically since its symptoms are similar to those of other esophageal disorders, such as gastroesophageal reflux disease (GERD).[2] The clinical signs of EOE differ depending on the age of the patient when they present. The manifestation of EOE differs between paediatric and adult patient populations. Food refusal, failure to thrive, gastrointestinal pain, heartburn, regurgitation, and vomiting are common symptoms in young children. Recurrent dysphagia and bolus blockage become the most significant symptoms in teenagers and adults. Spontaneous perforation with bolus blockage has been recorded in a few occasions.[3]

Indeed, EOE is generally recognised as the most common cause of bolus blockage and spontaneous esophageal perforation. It is evident that EOE patients' quality of life is limited depending on the severity of their disease, not only due to the burden of their symptoms but also due to the changes they must make to their diet, their social habits, and the challenges of coping without knowing the specific cause of their symptoms. Upper endoscopy with mucosal biopsies taken not just from the oesophagus but also from the stomach and duodenum to rule out other sites with eosinophilic infiltration is the gold standard for diagnosing EOE. According to recent United European Gastroenterology (UEG) guidelines, six biopsy specimens from various sections of the oesophagus should be collected, with specific attention given to conspicuous lesions. If an eosinophil-predominant inflammation in any esophageal biopsy is verified histologically [>15 eosinophils per high power field (hpf); >48 eosinophils per mm hpf] and other evident causes of eosinophilic eosinophilia are ruled out, the diagnosis of EOE is obtained.[2, 3]

For the initial therapy of EOE, current UEG guidelines propose swallowing topical corticosteroids (STC), high-dose PPI, or an elimination diet. The European Medicines Agency approved the orodispersible budesonide tablet for esophageal targeting in 2018 for induction treatment of adult EOE patients. It is now available in the majority of European countries.[4]

Oral medication administration is preferred due to its ease of administration, non-invasiveness, adaptability, patient compliance, and acceptability. Solid dosage forms, such as tablets, are easier to handle, stable, and ensure patient compliance. However, many elderly, young, and noncompliant patients struggle with traditional oral dosage forms, affecting 50% of the population. This issue is exacerbated by the increasing percentage of older people and the prevalence of dysphagia, eosinophillic esophagitis, and other medical issues. Tablets are primarily concerned with size and potential choking hazards, making them more susceptible to swallowing medications. Oral fast disintegrating drug delivery systems were created in the late 1970s to address these issues. These systems dissolve or disintegrate in the mouth without water in around three minutes, and are now gaining popularity as a new medication delivery technology due to improved patient compliance.[5]

Fast-dissolving films and mouth-dissolving tablets are used for oral fast-dissolving doses, but mouth-dissolving tablets have drawbacks like choking and mouth residues. A new drug delivery system called Fast dissolving films/oral dispersible film/mouth dissolving films/oral disintegration film/oral dissolving film was developed to address these issues. This thin, postage stamp-sized film is applied to the patient's tongue or mucosal tissue, absorbing saliva to hydrate the area. The film quickly dissolves and disintegrates, releasing the medication for absorption by the oral mucosa. The film's large surface area allows for rapid dissolving action in moist oral environments. The fast dissolving drug delivery system (FDDS) is a new generation of drug delivery technology developed in the late 1970s to address the difficulty of swallowing traditional solid dosage forms for patients with geriatric and elderly conditions. FDDS combines the benefits of tablet and liquid formulation technologies, making it easier to administer and improve patient compliance. The delivery mechanism, a thin oral strip, is placed on the patient's tongue or mucosal tissue, where it is rapidly wetted by saliva. Initially introduced in the confectionery industry in 2001, FDDS have expanded into food packaging and drug delivery. The film hydrates quickly at the application site, allowing for oro-mucosal absorption. The dissolve time for orally dissolving films is typically 5 to 20 minutes, depending on the polymer used. The rapid onset of action occurs within seconds, as the medication is absorbed oro-mucosally and bypasses first-pass metabolism to reach the systemic circulation.[6, 7, 8]

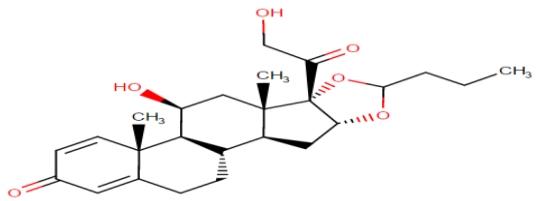


fig no.1:structure of budesonide

Budesonide is a glucocorticoid steroid with a pregna-1,4-diene structure that is strongly oxygenated. It is primarily used to treat asthma and non-infectious rhinitis, as well as to treat and prevent nasal polyposis. It functions as an anti-inflammatory agent, a bronchodilator, and a drug allergen. Freely soluble in dichloromethane; sparingly soluble in ethanol(95%). Budesonide had an absolute systemic availability of 6% to 13% following administration by mouth in healthy people, and the peak plasma concentration was reached in 1 to 2 hours, 80–90% of budesonide is metabolised in the first pass, for treatment of Eosinophilic Esophagitis – 1 mg twice daily for 6 to 12 weeks, this properties make it suitable for administration by oral route. This route of administration addresses the issue of poor oral bioavailability by avoiding the drug's presystemic metabolism.[9, 10]

MATERIALS AND METHODS

Budesonide was purchased from Vamsi Labs Ltd. Solapur, India. HPMC E 15 LV was purchased from Loba Chemie Pvt. Ltd. Mumbai, India. Citric acid, Sodium starch glycolate, sucralose, and methanol was from Research-Lab Fine Chem Industries, Mumbai, India. All chemical compounds utilised were of analytical grade.

Selection of polymer:[11]

HPMC E 15 LV, Xanthan gum, and maltodextrin film-forming polymers were tried for the formulation of films. Different concentrations of the polymers were used alone for prepration. Following preparation, the films were tested for lack of whiteness and opacity as well as for good folding endurance and quick disintegration.

Selection of plasticizer:[11,12]

Plasticizer that imparts mechanical strength, elasticity, elongation, folding endurance, and tensile strength to the polymer and is effective in increasing the glass transition temperature of the film. Science Direct Journal was used for this literature search. PEG 400 a suitable plasticizer, was chosen after extensive literature search.

Drug-Excipient compatability study:[13]

By mixing a small amount of dried potassium bromide with the respective excipients, the FT-IR of BUD and HPMC E 15 was determined. This mixture was then run through FTIR (JASCO- FT/IR-4100) to obtain an IR spectra.

Method of preparation of orodispersible film of budesonide:[2,14,15,16]

The orodispersible films were prepared by solvent casting. Various polymers were used as film-forming polymers. The orodispersible films were prepared by dissolving drug in the mixture of solvent (methanol and water) in the beaker, and other ingredients were added one by one. Finally, polymer was added, and stirring was carried out on a magnetic stirrer for 20–30 minutes. The mixture was kept on an ultrasonicator for 5 minutes to remove entrapped air bubbles. The solution was cast on a Petri plate and then kept in a hot air oven at 60°C for 24 hours. The films were carefully peeled from the Petri plate, checked for flaws, and cut to the size needed for testing (square film: 2 cm length, 2 cm width) and stored in a dessicator until use.

Factorial design:[17]

Using the commercially available software package Design-Expert® version 13. 3^2 factorial designs were implemented for optimization of Budesonide ODF that contained two independent variables at three levels +1, 0 and -1. The 3 levels were decided on the basis of trial batches and their evaluation. The difference between 2 consecutive levels was kept same. The levels and the exact concentration of the variables used in different formulations are shown in Table no 1 respectively. Accordingly, total nine formulations were designed and the compositions of different formulations have been depicted in Table no 2. The different independent variables include: Plasticizer i.e PEG 400 (X1) & Polymer i.e HPMC E 15 LV (X2). The batches were analysed, and the effect of each individual variable was investigated using response surface methodology. The different dependent responses include: in vitro disintegration time, in vitro drug release.

Table no 1: Factorial design factors and responses

Independent variables	-1	0	+1
X1= amount of HPMC E 15 LV (mg)	550	600	650
X2= amount of PEG 400 (ml)	0.75	1	1.25
Dependent variables			
Y1 = Disintegration time			
Y2 = In vitro drug release (%)			

Table no 2: Factorial batches of BUD orodispersible film

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Drug (mg)	16								
HPMC E 15 LV (mg)	550	600	650	550	600	650	550	600	650
PEG 400 (mg)	0.75	0.75	0.75	1	1	1	1.25	1.25	1.25
Citric acid (mg)	5	5	5	5	5	5	5	5	5
Sucralose(mg)	5	5	5	5	5	5	5	5	5
SSG (mg)	2	2	2	2	2	2	2	2	2
Methanol (ml)	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6
Water (ml)	Q.S	Q.S	Q.S	QS	Q.S	Q.S	Q.S	Q.S	Q.S

EVALUATION OF FILMS

1. Physical appearance:[18]

The physical appearance and surface texture of the prepared ODFs were assessed simply through visual inspection of the films and texture evaluation by feel or touch.

2. Thickness measurement:[19]

The thickness of the films is essential to be uniforms as it is directly associated by to the precision of the dose. Thickness of all prepared ODFs containing budesonide were measured by using standard vernier caliper. Five films from each batches were picked randomly and thickness was measured individually.

3. Weight variation:[20]

Individual ODFs were weighed for weight uniformity, and average weights were computed. The average weight of the films is then subtracted from the individual weights of the films. A considerable variance in weight implies the inefficiency of the method used and the possibility of non-uniform drug content.

4. Folding Endurance:[21]

The number of folds necessary to break the specimen or create visible fissures is denoted as folding endurance. This demonstrates the film's brittleness. This test was performed on 2cm×2cm films by folding the film at the same location many times until a breakage was observed.

5. Surface pH:[22]

The orodispersible film's surface pH is calculated to evaluate the probability of any in vivo adverse effects, as acidic or alkaline pH may cause irritation or inflammation to the oral mucosa, and it is assessed to keep the surface pH as close to neutral as possible. The film was placed in a petri plate and slightly moistened with 1 ml of distilled water for 30 seconds before measuring pH by bringing the electrode contacting the film's surface and allowing it to stand.

6. Drug content uniformity:[23]

Drug content uniformity was determined by dissolving the film (2×2 cm2) in 100 ml of methanol in 100 ml of volumetric flask. Then the content were stirred on a magnetic stirrer, until the film dissolved. Then 5ml solution was taken and diluted, and the resulting solution was filtered through Whatman filter paper. The drug content was determined after proper dilution at 245nm using UV Vis spectrophotometer.

7. In vitro disintegration time:[24]

The disintegration time was measured using the petridish method and is defined as the time (in seconds) at which a film begins to break or disintegrate. After placing the film in a petridish and adding 2 ml of phosphate buffer 6.8, the petridish was shaken constantly to determine the time at which the film began to break or disintegrate. The time it took to disintegrate the film was examined.

8. In vitro dissolution study:[25]

The dissolution study was carried out using USP 1 apparatus at 370C ± 0.50C using 900 ml of Phosphate buffer (pH 6.8). The rotation of the basket at 50 revolutions per minute. The drug loaded film (2cm×2cm) was placed in medium. 2 ml samples were withdrawn at 1, 2, 3, 4, and 5 minutes and were filtered through Whatmann Filter paper and analysed spectrophotometrically at 245nm . An equal volume of fresh dissolution media, maintained at the same temperature, was added after withdrawing the sample to maintain the volume.

9. Accelerated stability study:[26]

The optimized formulation's stability studies were carried out in accordance with ICH Q1A (R2) guidelines. For two months, the formulations were packaged in aluminium foil and placed in a self-sealing bag at 40 ± 2°C and 75 ± 5% RH and examined for any changes in appearance, weight variation, drug content, drug release, disintegration time, and surface pH.

RESULT AND DISCUSSION

The current study sought to formulate and evaluate a budesonide orodispersible film. Preliminary trials were conducted to evalute various excipients in order to select the best excipient.

Selection of polymer:

Polymers are selected based on their ability to make clear, transparent, non-sticky, and flexible films. In the preliminary trials, HPMC E 15 LV, Maltodextrin, and Xanthan gum film-forming polymers were used. Air bubble entrapment was detected in xanthan gum, making it difficult to peel from a petri plate, and stiffness was observed in maltodextrin. The films produced with HPMC E15, on the other hand, had neither whiteness nor oiliness and were easy to peel from the petri plate. As a result, HPMC E15 was selected as a suitable polymer for the formulation.

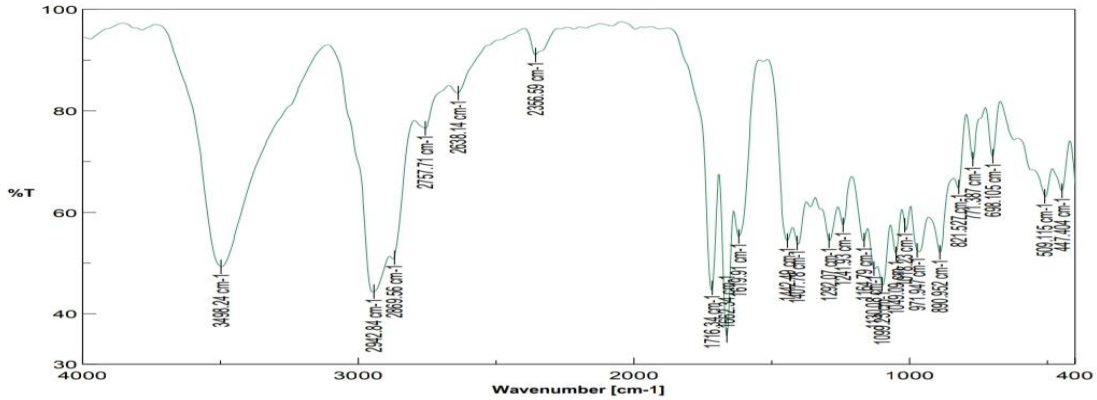
Selection of plasticizer:

Flexibility is a crucial consideration while preparing an oral film. The plasticizer used determines the film's flexibility. The plasticizer grades used in the trial were PEG 200 and PEG 400. There was no whitening noticed in the PEG 200-formulated film; however, the

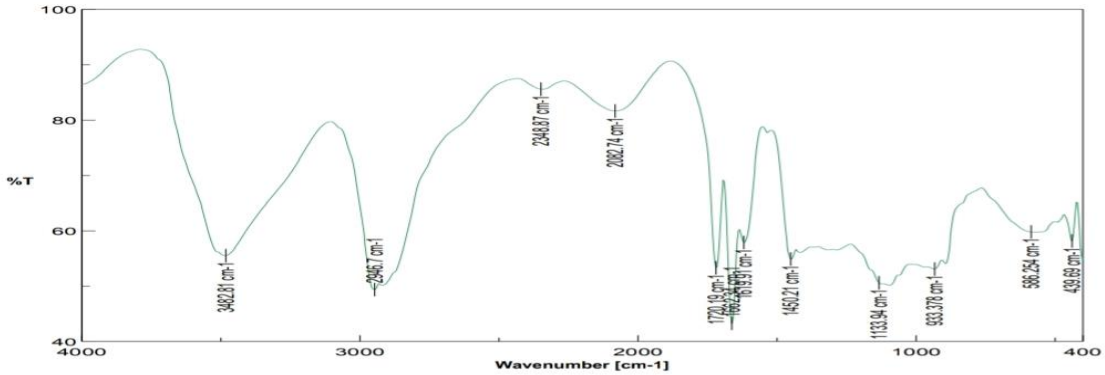
folding endurance value was found to be low. The PEG 400 film showed good folding endurance, and no whitening was noted. As a result of these findings, PEG 400 was chosen for the formulation.

Drug-Excipient Compatabilty study:

Due to no change in the peak, the FT-IR of BUD reveals the absence of interaction between BUD and Excipients.



(A)



(B)

Fig no.2: (A) FTIR of budesonide, (B) FTIR spectra of budesonide with HPMC E15 LV

The physical parameters such as thickness, weight variation, folding endurance, surface pH, disintegration time, % drug content, and in vitro drug release of the optimisation batches of orodispersible film (Table 2) were examined. The results of the evaluation are given in Table no 3.

1. Physical appearance:

The essential parameters for visual assessment are clarity, transparency, and oiliness. The films were discovered to be clear and transparent in appearance, indicating film homogeneity. The film was non-oily, which helped to avoid the film sticking during administration. The films had a smooth surface and were appealing to look at. Thus clear, transparent, and non-oily films were obtained, and further testing was performed.

2. Thickness:

The thickness of the budesonide orodispersible film was measured with a standard vernier calliper, and the average thickness of all films is shown in Table no 3. The thickness has been determined to be in the range of 0.078 to 0.087. The thickness of the films increased as the concentration of polymers increased. The estimated standard deviation values are all very low in each case, indicating that the formulated films were uniform in thickness. Table no 3 shows the results.

3. Weight variation:

Table no 3 shows the average weight of all films after determining the weight of budesonide orodispersible films using a weigh balance. The weight of the films was determined to be between 74.4 to 98.6 mg for all batches (F1-F9). Because of the polymer content, the formulation F1 had the lowest weight. In all cases, the calculated standard deviation values are quite low, indicating that the manufactured films were of uniform weight.

4. Folding endurance:

The folding endurance of budesonide ODFs was determined by folding a small film of formulation repeatedly until it broke, and the average folding endurance of all films is shown in table no 3. It was found between 122 to 156. Folding endurance indicates the

brittleness of the films. It was discovered that when polymer concentration increases, so does folding endurance. The results are shown in a table no 3.

Table no 3: Evaluation parameters for factorial batches F1-F9.

Factorial Batches	Thickness (mm)	Weight Variation (mg)	Folding Endurance	Surface pH	% Drug Content	Disintegration time (sec)
F1	0.078	74.4	122	6.34	98.31	60
F2	0.081	78.2	135	6.30	91.77	51
F3	0.083	83.5	140	6.55	96.85	55
F4	0.079	84.8	129	6.27	94.93	54
F5	**0.082**	**90.7**	**142**	**6.21**	**99.22**	**43**
F6	0.086	98.6	152	6.36	93	47
F7	0.080	88.1	133	6.62	80.53	58
F8	0.083	95.4	148	6.60	92.35	46
F9	0.087	96.8	156	6.42	95.55	49

Table no 4: Cumulative % Drug Release of factorial batches.

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	**0**	0	0	0	0
1	30.1	32.41	35.10	28.81	**39.02**	26.28	23.81	40.01	37.81
2	39.21	45.02	49.52	40.81	**52.13**	39.90	37.68	55.61	57.21
3	59.32	62.72	69.41	58.61	**78.28**	60.72	65.58	79.16	76.18
4	76.82	82.19	85.23	78.20	**87.20**	79.88	78.55	87.80	83.24
5	87.02	90.85	89.01	89.65	**98.82**	95.72	87.81	96.62	92.74

5. Surface pH:

Given that an acidic or alkaline pH might irritate the oral mucosa and alter polymer hydration, the surface pH of the film was determined to optimise drug penetration and is shown in the table no 3. A pH meter was used to determine the surface pH of the budesonide orodispersible film. It was discovered between 6.21 to 6.62. The pH of the surface was kept as close to salivary pH as practicable.

6. Drug content uniformity:

The drug content uniformity of budesonide orodispersible films was determined to be in the range of 80.53 to 99.22 as shown in Table no 3, F7 had the least amount of drug content, whereas F5 had the most. This could be due to the high concentration of drug dispersed inside the formulations or vice versa. The results are shown in a table no 3.

7. In vitro disintegration time:

The disintegration time of budesonide orodispersible films in vitro was reported to be between 43 and 60 seconds. Formulation F5 has the fastest disintegration time. The results are shown in a table no 3.

8. In vitro dissolution time:

All budesonide orodispersible films were tested for in vitro drug release using a USP Type II (basket) dissolution test apparatus and phosphate buffer pH 6.8 as a medium. A 300-second in vitro drug release study was carried out. In-vitro drug release studies indicated that all formulations released the drug quickly. Over a 5-minute period, maximum in-vitro release was found to be 98.82% in batch F5, while minimum in-vitro release was found to be 87.02% in batch F1. The table no 4 shows results of the release studies. Figure no.3 depicts a graph plotting % cumulative percentage drug release versus time.

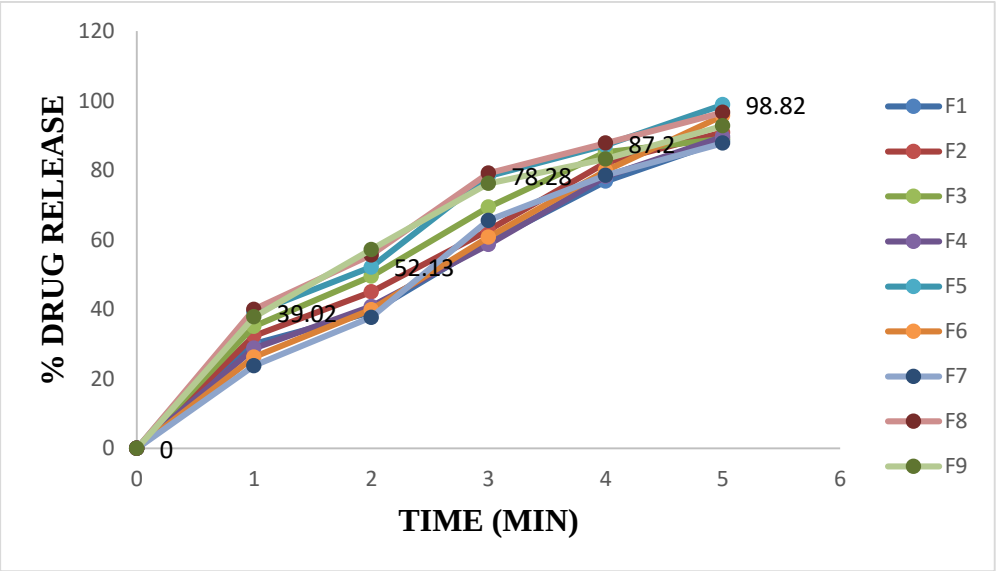


Fig no 3: Cumulative % drug release of factorial batches

Regression analysis:

1. Effect of formulation variables on disintegration time:

The Quadratic model was found to be significant with an F value 353.40 (P= 0.0002). In this case X1, X2, X1X2 was found to be significant and the model describes the disintegration time. The factorial equation for disintegration time (Y1) can be represented by following equation.

Disintegration time(Y1) =+1160.55556-3.430 X1-126.0 X2-0.080 X1 X2+0.0028 $X1^2$ +82.667 $X2^2$

With increase in HPMC E15 LV concentration budesonide ODF disintegration time was found to be increase due to the combined effect of X1 & X2 has been shown on the response surface plot also known as counter plot (Figure No 4). The HPMC E15 conc.(factor X1) & PEG 400 ratio (factor X2)exerted positive effect on disintegration time (Y1), means magnitude of these factors increase disintegration time. The Contour plot gave an idea about the effect of formulation variables on disintegration time (Y1). From the counter plot the best factorial batch was determine. The Figure No.5 shows a graph of observed verses predicted values.

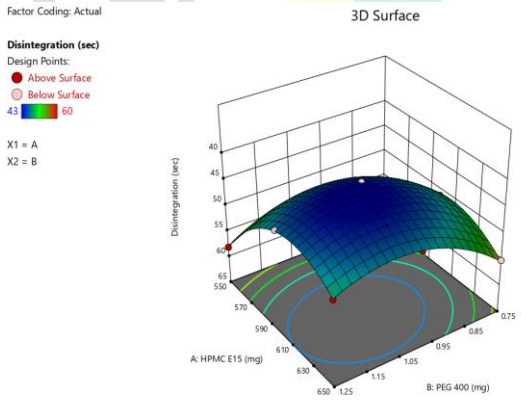


Fig no 4: Response surface plot showing effect of formulation variables on disintegration time (Y1)

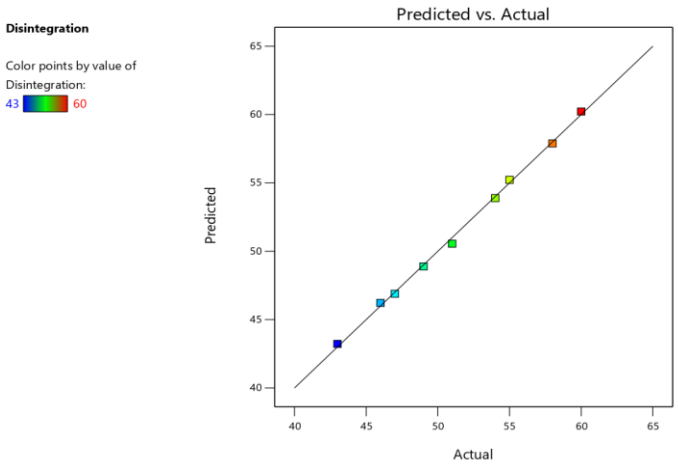


Fig no 5: Correlation between actual and predicted values for disintegration time (Y1)

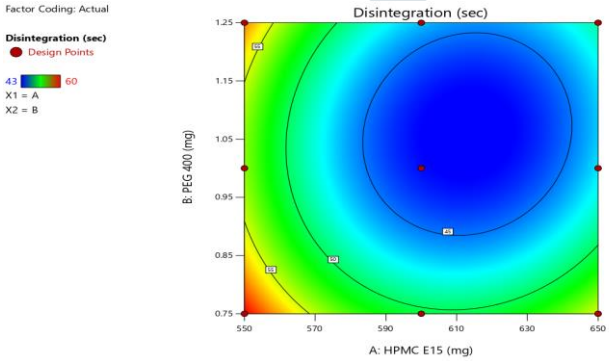


Fig no 6: Contour plot showing effect of formulation variables on disintegration time in sec (Y1)

2. Effect of formulation variables on cumulative % drug release at 5 min:

The Quadratic model was found to be significant with an F value 10.72 (P= 0.0395). In this case X1, X2, X1X2 was found to be significant and the model describes the cumulative %t Drug release at 5 min. The factorial equation for percentage Drug release at 5 min (Y2) can be represented by following equation.

% Drug release (Y2) = -699.42667+2.4349X1+101.340X2+0.0588X1 X2-0.002042 X12-64.88X2 2

With increase in HPMC E15 LV concentration BUD drug release rate was found to be increase due to the combined effect of X1 & X2 has been shown on the response surface plot also known as counter plot (Figure No.7). The HPMC E15 LV conc.(factor X1) & PEG 400 ratio (factor X2)exerted positive effect on drug release at 5 min (Y2), means magnitude of these factors increase cumulative % drug release. The Contour plot gave an idea about the effect of formulation variables on percent drug release at 5 min (Y2). From the counter plot the best factorial batch was determine. The Figure No.8 shows a graph of observed verses predicted values.

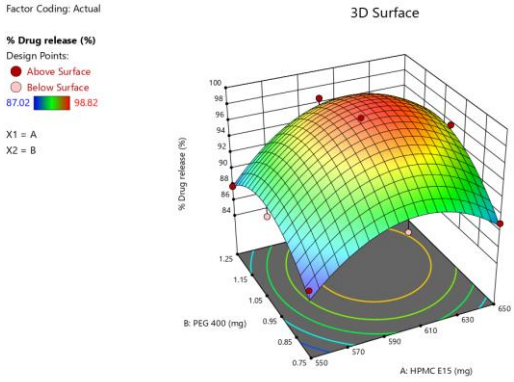


Fig no 7: Response surface plot showing effect of formulation variables on percent drug release (Y2) at 5 min

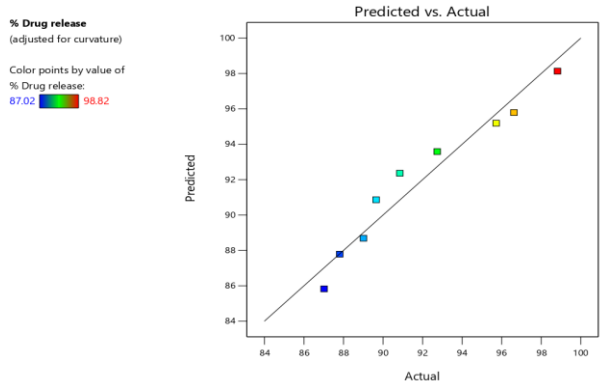


Fig no 8: Correlation between actual and predicted values for cumulative % drug release at 5 min (Y2)

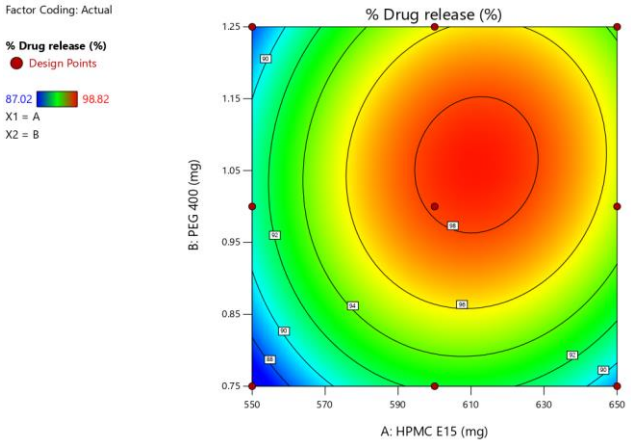


Fig no 9: Contour plot showing effect of formulation variables on cumulative % drug release at 5 min (Y2)

Table no.5: Data of ANOVA study for dependent variables from 3^2 factorial designs

Source	d.f.	Mean square	Sum of squares	F value	Probability
Response (Y1) = Disintegration time (sec)					
A-HPMC E15	1	73.50	73.50	496.13	0.0002
B-PEG 400	1	28.17	28.17	190.13	0.0008
AB	1	4.00	4.00	27.00	0.0138
A^2	1	102.72	102.72	693.38	0.0001
B^2	1	53.39	53.39	360.38	0.0003
Response (Y2) = % Drug release					
A-HPMC E15	1	28.12	28.12	11.34	0.0435
B-PEG 400	1	17.65	17.65	7.12	0.0758
AB	1	2.16	2.16	0.8715	0.4194
A^2	1	52.12	52.12	21.02	0.0195
B^2	1	32.89	32.89	13.26	0.0357

Table no.6: Data of ANOVA study

Source	d.f.	Mean square	Sum of squares	F value	Probability
Response (Y_2) = %Drug Release					
Model	5	132.94	26.59	10.72	0.0395
Residual	3	7.44	2.48	-	-
Total	8	140.38	-	-	-
Response (Y_1) = %Disintegration time					
Model	5	261.78	52.36	353.40	0.0002
Residual	3	0.4444	0.1481	-	-
Total	8	262.22	-	-	-

Optimization:

The formulation of nine batches of oral films was carried out using a 3^2 factorial design. The formulation batches were tested for a variety of physicochemical parameters. After assessing the data and entering the results into design expert software, batch F5, comprising 600 mg of HPMC E15 LV and 1 ml of plasticizer, was suggested as the optimised batch. The optimised films disintegrated in 43 seconds and released approximately 98.82% of the drug in 5 minutes.

9. Stability study:

The stability studies for the optimised batch were carried out and the results of the assessment are shown in Table no 7. Stability studies reveal no significant differences in appearance, weight variation, or thickness. There are no differences in drug content, surface pH, disintegration time, or drug release. As a result, it implies that the formulation is both physically and chemically stable.

Table no 7: Stability studies

Time (day)	Thickness (mm)	Surface pH	% Drug content	Disintegration time	% Drug release
30	0.083	6.22	99.18	42	98.80
60	0.083	6.12	99.07	41	98.65

CONCLUSION

The study aimed to develop a budesonide orodispersible film for treating eosinophilic esophagitis, overcoming liver metabolism disadvantages and improving bioavailability. The conventional formulation has average bioavailability and patient noncompliance. To improve bioavailability and reduce side effects, a solvent casting technique was used. A preformulation study revealed maximum absorption at 245 nm of budesonide. Drug-excipient compatibility studies confirmed drug-compatible polymers and excipients.

The solvent casting technique was used to formulate the orodispersible films. The formulation with HPMC E15 LV combined with PEG 400 as a plasticizer demonstrated outstanding in vitro disintegration time and cumulative percent dissolution. After evaluating various batches, the F5 batch produced the desired results, releasing nearly 98.82% of the medication in just 5 minutes. The optimized formulation F5 was found to be stable at accelerated stability conditions. Based on the above discussion, it is possible to conclude that the formulation and optimisation of orodispersible budesonide films employing HPMC E15 as a film-forming polymer and PEG 400 as a plasticizer was effective. As a result, budesonide can now be administered orally as films to treat Eosinophilic esophagitis.

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