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Research Article

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Design of Fast Dissolving Anti-Asthmatic Films Using 2^3 Factorial Designs

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Abstract Fast dissolving films are playing an important role in the current pharmaceutical drug delivery systems. They have convenience and ease of use over solid and liquid dosage forms. In the present research, fast dissolving oral film of terbutaline sulphate were developed using HPMC K15 LV as film forming polymer. The films were prepared by solvent casting method. Optimization of HPMC E15 LV, SSG and PEG-400 was carried out using 2^3 full factorial designs. The formulated films of terbutaline sulphate were evaluated for their physico-mechanical parameters like disintegration time, tensile strength, percent elongation, folding endurance and *In-vitro* drug release. Estimation of drug content uniformity of terbutaline sulphate films was performed and the results were satisfactory. Optimized batch F_6 has thickness (0.254±0.01mm), disintegration time (19.90±0.42 sec.) tensile strength (2.95±0.09 Mpa), % Elongation (18.95±0.12), Folding endurance (153±7.0), CPR_{1min} 35.16±4.56% and CPR_{10min} 80.29±4.15%.

Keywords Fast dissolving film, asthma, terbutaline sulphate, 2^3 factorial design, first pass effect.

Introduction

Oral route is a most preferred route of drug administration for systemic effect due to its ease of administration, non-invasiveness, adaptability, patient compliance and acceptability [1]. About 60% of all the formulations are solid dosage form. Tablet is the most preferred dosage form due to ease of manufacturing, transportation and more patient compliance [2]. Generally geriatric, pediatric, nauseous, bed ridden and non-compliance patients experience difficulties in swallowing the conventional oral dosage form and do not take their medicines as prescribed. It is estimated that 50 % of the population was affected by this problem, which finally results in a higher chance of non-compliance & ineffective therapy [3].

The elderly constitute a major portion of today's population mainly because of increased life expectancy of individuals[4]**.** Dysphagia or difficulty in swallowing is common problem, the disorder of dysphagia is associated with many medical conditions including stroke, Parkinson's disease, AIDS, thyroidectomy, head and neck radiation therapy and other neurological disorders including cerebral palsy [5]**.** The most common complaint with tablet is size, fear of chocking followed by surface form and taste. The problem of swallowing tablets is more evident in geriatric and pediatric patients, as well as travelling patients who may not have ready access to water [6].

To overcome this Oral fast disintegrating drug delivery systems were developed, these systems were first developed in the late 1970s as an alternative to tablets, capsules and syrups for pediatric & geriatric patients who experience difficulties in swallowing traditional oral solid dosage forms. These dosage forms either dissolve or disintegrate generally within a 3 minute in mouth, without need of water. Oral fast Disintegrating dosage form have started gaining popularity & acceptance as new drug delivery system because they are easy to administer & lead to better patient compliance [7]**.**

Oral fast disintegrating dosage form mainly consist of oral disintegrating tablets which disintegrate rapidly, usually within a matter of seconds, when placed upon the tongue but leave residues in mouth which causes feeling of grittiness in mouth. Even with fast dissolving tablets there is a fear of choking due to its tablet type appearance. One study showed that 26% of 1576 patients experienced difficulty in swallowing tablets. The most common complaint was tablet size, followed by surface form and taste. To overcome problems of mouth dissolving tablets, a new drug delivery system for the oral delivery of the drugs, was developed which is known as Fast dissolving films/mouth dissolving films/oral dispersible film/oral dissolving film/oral disintegrating film [8]**.**

Fast dissolving oral films is a type of oral drug delivery system for the oral delivery of the drug which was developed based on the technology of the transdermal patches [9]. This delivery system consists of a thin film of the size of a postage stamp, which is placed on the patient's tongue or mucosal tissue, where it instantly hydrates by absorbing saliva; the film then rapidly disintegrates and dissolves to release the drug for oral mucosal absorption. This fast dissolving action is primarily due to the large surface area of the film, which wets quickly when exposed to the moist oral environment [10]. Fast dissolving oral films were initially introduced in the market as breath fresheners and personal care products such as dental care strips and soap strips. However, these dosage forms were introduced in the United States and European pharmaceutical markets for therapeutic benefits.

The first of the kind of fast dissolving films were developed by the major pharmaceutical company Pfizer who named it as Listerine pocket packs™ and were used for mouth freshening. Chloraseptic® relief strips were the first therapeutic fast dissolving oral thin films (OTF) which contained benzocaine and were used for the treatment of sore throat. Technology Catalysts forecasts the market for drug products in oral thin film formulations was valued of $500 million in 2007 and could reach $2 billion in 2012. Based on upward global growth trends of the past decade, the fast dissolving dosage market could produce revenues of $13 billion by 2017 [11].

Special features of fast dissolving oral films [12-14]

- Thin elegant film
- Available in various size and shapes
- Unobstructive
- Excellent mucoadhesion
- Fast disintegration and dissolution
- Rapid drug release
- Bypasses first pass effect

Material and Methods

Terbutaline sulphate was obtained as Gift sample from Bioplus Life Science, Banglore, PEG-400, Tween-80, Tween-80, Citric acid, Methanol were purchased from Thomas baker, HPMC E15LV and aspartame purchased from Loba Chem, sodium starch glycolate (SSG) was purchased from S.D. Fine, Mumbai. Design expert® software 10 trial version was used.

Determination of Wavelength Maxima (λ_{max}): Accurately weighed 10 mg of drug was dissolved in 10 ml of 6.8 pH Phosphate Buffer in a 10 ml volumetric flask. 0.1ml of this stock solution was pipetted into a 10 ml volumetric flask and volume made up to the mark with same buffer. The resulting solution was scanned between 200-400 nm using UV-Visible double beam spectrophotometer [15].

Preparation of Calibration Curve of Terbutaline Sulphate[9]

(a) Preparation of Buffer 6.8 gm of KH_2PO_4 and 0.9 gm of NaOH dissolved in 1000ml of distilled water gave the pH buffer 6.8.

(b) Calibration curve in phosphate buffer pH 6.8: 10 mg of Terbutaline sulphate was weighed accurately and dissolved in 5 ml of buffer in a 10 ml of volumetric flask and volume was made up to 10 ml with the phosphate

buffer pH 6.8. Aliquot of 1 ml of this solution was withdrawn and transferred to 10 ml volumetric flask and diluted to 10 ml with pH 6.8 phosphate buffer to obtain a stock solution of 10μg/ml. From this stock solution, aliquots of 0.5ml, 1.0ml 1.5ml 2.0ml and 2.5ml were transferred to 10 ml volumetric flasks and volume was made up to 10 ml phosphate buffer pH 6.8. The absorbance of these solutions was measured at 276 nm against a blank phosphate buffer pH 6.8. The calibration curve was obtained by plotting the absorbance of terbutaline versus the concentration of terbutaline. The straight line of best fit was obtained by using linear regression analysis program.

FTIR Spectra of terbutaline sulphate: IR spectra of physical mixture of drug and excipients were recorded by KBr pellet method using Fourier Transform Infrared Spectrophotometer. A base line correction was made using dried potassium bromide pellet. The potassium bromide-drug pellet of approximately l mm diameter was prepared by grinding 3-5 mg of physical mixture of drug-excipients with 100-150 mg of potassium bromide in pressure compression machine. The sample pellet was mounted in IR compartment and scanned at wavelengths 4000 cm^{-1} to 400 cm^{-1} [16].

Formulation development of fast dissolving oral film [17]

The solvent casting method was used for the preparation of the fast dissolving oral films. From the preliminary physical observation of the films prepared during initial trials, the best compositions were used for the incorporation of drug. The required amount of film forming polymer was allowed to hydrate in 1/3 amount of water for about 6 hours and then it was uniformly dispersed to get clear solution of film forming polymer to this required amount of plasticizer was added. Drug and other ingredients such as superdisintegrant, sweetener, wetting agent, saliva stimulating agent and colour were dissolved one by one in other 1/3 amount of water with constant stirring to form clear aqueous solution. Menthol was dissolved in alcohol and then added to second portion of solution.

All the solutions were then mixed and remaining water is also added to the solution. The final prepared solution was sonicated to remove all the entrapped air bubbles. The final solution (10 ml) was poured in a glass mould having area of $75cm^2$ kept on a leveled surface in hot air oven and dried at 30^0c temperature for 24 hours. The film thus formed was carefully removed from the moulds and were cut into size of 3*2 cm. Each containing ≈ 2.5 mg of terbutaline sulphate. The films were wrapped in aluminum foil and stored in airtight plastic bags till further use.

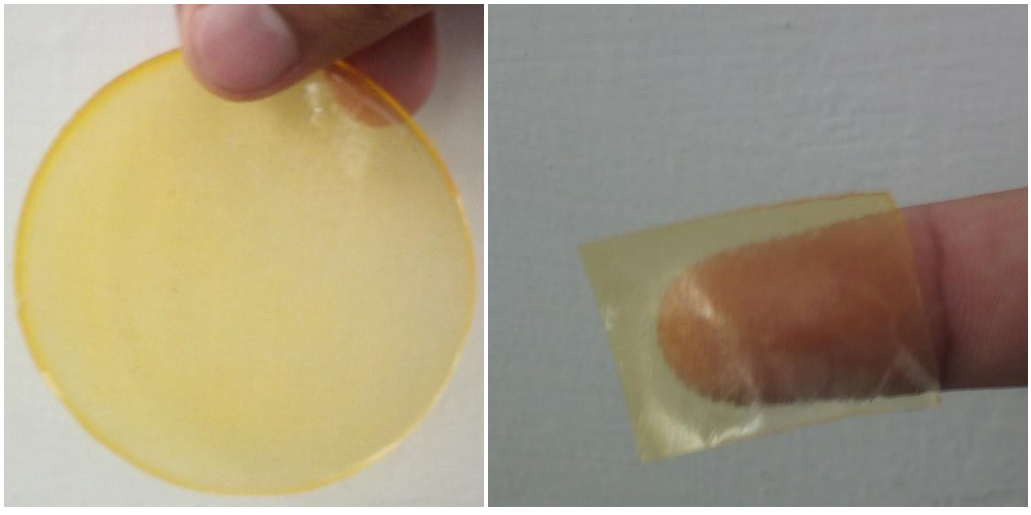

Figure 1: Fast dissolving oral films of Terbutaline sulphate

2^3 factorial design [19]

Regular 2 level factorial designs for 3 factors was employed to study the effects of independent variables X1(HPMC E15LV), X2 (sodium starch glycolate) and X3 (polyethylene glycol-400) over the independent variables like

disintegration time, tensile strength, folding endurance, percent elongation and cumulative drug release at 10 minutes as shown in layout Tables 1-2. In this design three factors were evaluated each at two levels (-1 and+1) and all possible eight experimental batches were formulated. Composition of all eight possible combinations of fast dissolving oral films of terbutaline sulphate using 2^3 full factorial designs is shown in Table 2. A multiple linear regression equation containing interactive and polynomial terms was used to calculate the response as follows $Y=bo+b_1X_1+b_2X_2+b_3X_3+b_1X_1X_2+b_2X_2X_3+b_3X_2X_3+b_{123}X_1X_2X_3$…..

Table 1: List of variables employed in 2^3 factorial designs

Factors	**Levels**	
	Low (-1)	**High (+1)**
Terbutaline sulphate (mg)	30	
HPMC E15LV(%w/v)	3.0	5.0
SSG (%w/w)	2	8
PEG-400 (%w/w)	10	30
Tween-80(%w/v)	0.5	
Citric acid(%w/v)	0.5	
Aspartame(%w/v)	0.3	
Menthol(%w/v)	0.1	
Alcohol (ml)	1	
Flavour	0.1	
Colour	qs.	
Distilled water (ml)	10	

Table 2: Preparation of fast dissolving oral films on the basis of 2^3 factorial designs

Formulation code	**HPMC E15LV (%w/v)**	**SSG (%w/w)**	**PEG-400 (%w/w)**	**HPMC E15LV (%w/v)**	**SSG (%w/w)**	**PEG-400 (%w/w)**
	Levels			**Actual amount**		
F1	-1	1	-1	3	8	10
F2	-1	1	1	3	8	30
F3	-1	-1	1	3	2	30
F4	-1	-1	-1	3	2	10
F5	1	-1	-1	5	2	10
F6	1	1	1	5	8	30
F7	1	1	-1	5	8	10
F8	1	-1	1	5	2	30

*Amount of Drug, Tween 80, Citric acid, Aspartame, Menthol, Alcohol, Flavour and colour was kept constant

Evaluation of Fast Dissolving Oral Films of Terbutaline Sulphate

The fast dissolving oral films formed were removed carefully, placed in vacuum oven and vacuum was applied to remove traces of solvent if any. They were stored in desiccators for further evaluation tests. Formulated films were then subjected for critical factors of fast dissolving oral films such as disintegration time, tensile strength, percentage elongation, folding endurance, surface pH, and *in-vitro* release studies.

Thickness:

The thickness of prepared films was measured using digital vernier caliper with a least count of 0.01 mm at five spots of the films. The thickness was measured at five different spots of the film, four at corners and one at center of film and average was taken. Data is represented as a mean± S.D.of five replicates [20].

Weight Uniformity:

For determination of film weight uniformity, three films each of 3*2 cm^2 of every formulation batch were taken and weighed individually on a digital balance. The average weights were calculated. Data is represented as a mean± S.D. of three replicates [21].

Disintegration Time:

Disintegration test was performed by placing the prepared film in the glass Petri dish containing 20 ml of 6.8 pH phosphate buffer. The time required for the film to complete disintegrate was recorded and results are expressed as mean of 3 determinations. Data is represented as a mean± S.D.of three replicates [22].

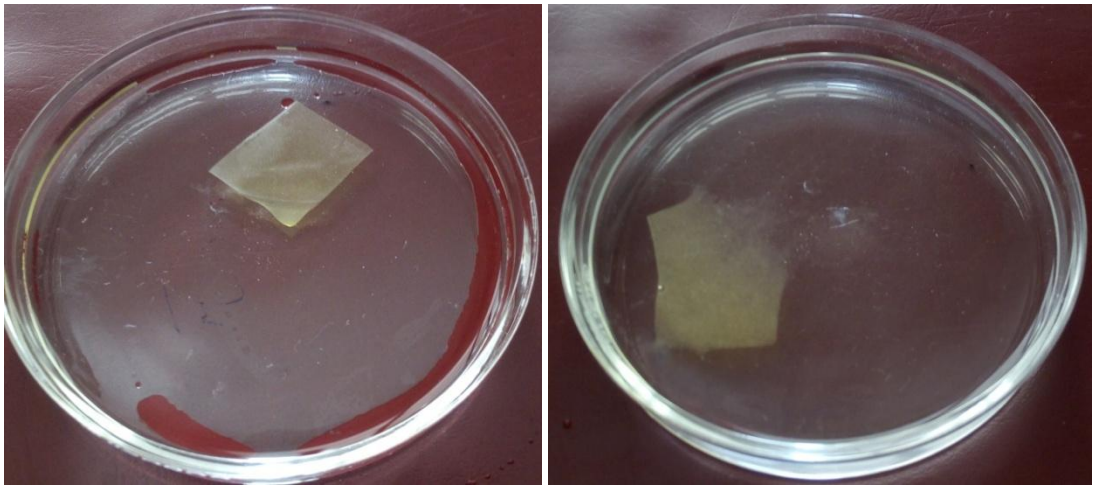

Figure 2: Disintegration of fast dissolving oral films of terbutaline sulphate in 6.8 P^H buffer

Folding Endurance:

Folding endurance of the films was determined manually by repeatedly folding each film at the same place till it broke. A film of (2 x 3 cm) was cut and repeatedly folded at the same place till it broke. The number of times of film could be folded at the same place without breaking gave the value of the folding endurance. Data is represented as a mean± S.D. of three replicates [21].

Drug Content Determination: The oral film of size 6 cm^2 was dissolved in 10 ml of phosphate buffer of P^H 6.8 and solution was filtered and drug content was estimated at 276 nm using double beam UV/Visible spectrophotometer. The experiments were carried out in triplicate for films of all formulations and average value was recorded as mean± S.D [21].

Surface pH

The films used for determination of their surface pH using universal digital pH meter. Film was wetted with deionized water and determines the surface pH with digital pH meter (Henna). The mean of three readings was recorded [20].

Tensile strength and % elongation

Mechanical properties of the film are important from packaging and patient handling point of view. Tensile test was performed to assess strength and elasticity of all film formulations. The elongation-to-break (also called ultimate elongation) is the strain on a material when it breaks and it gives an indication of toughness and stretch-ability prior to breakage. These parameters dictate the end-use handling properties and mechanical performance of the films. Casted films were cut into specimens of the specified size. Then 3 specimens were applied on tensile tester to

determine the tensile properties. The tensile strength is expressed in terms of Mpa and strain in terms of % elongation [23].

Tensile strength = (Load at failure×100) / (Strip thickness × Strip width)

% Elongation = (Increase in length of strip × 100) /Initial length of strip.

***In-vitro* dissolution study**

The release of drug from the prepared fast dissolving film into phosphate buffer pH 6.8 at 37 ± 0.5°C was performed using a six stage dissolution apparatus. Each fast dissolving film was keep to the vessel (900 ml capacity). Adequate sink conditions were provided by placing 200 ml of phosphate buffer pH 6.8 in each vessel. Dissolution paddle speed maintained at 50 rpm. After time intervals each of 1 minute from 1 minute to 10 minutes, 3 ml sample was withdrawn, filtered through a millipore filter of 0.45 µm pore size and assayed spectrophotometrically at λ_{max} 276 nm. Immediately after each sample withdrawal, a similar volume of phosphate buffer pH 6.8 was added to the dissolution medium to maintain the sink condition. The absorbance of the polymeric additives was negligible and did not interfere with λ_{max} of the drug [22].

Results and Discussion

Determination of wavelength maxima in phosphate buffer pH 6.8: The wavelength maximum for terbutaline sulphate in phosphate buffer pH 6.8 was found to be 276 nm (Figure 3). Terbutaline sulphate showed a linear relationship with correlation coefficient of 0.999 in the concentration range of 5-25 µg/ml in phosphate buffer pH 6.8.

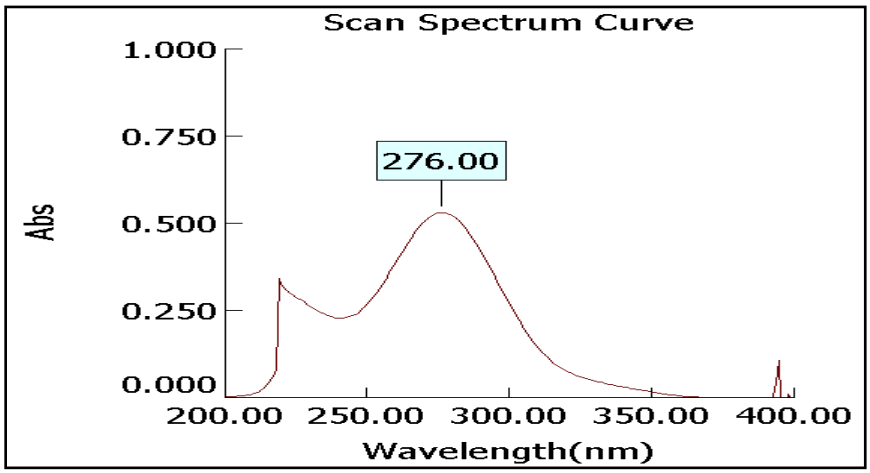

Figure 3: Wavelength maxima of terbutaline sulphate in phosphate buffer pH 6.8.

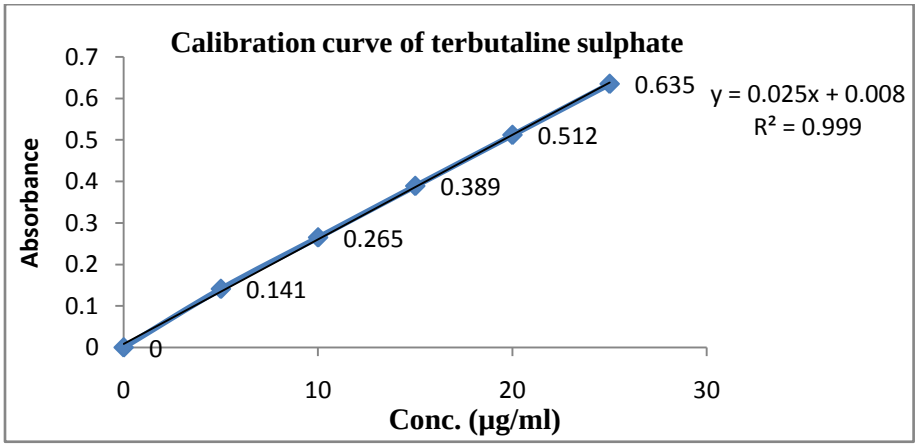

Figure 4: Calibration curve of TBS in phosphate buffer pH 6.8 at 276 nm

Table 3: Statistical parameters related to standard curve of Terbutaline sulphate

Media	Parameters	Values
Phosphate buffer pH 6.8	Beer's Law Range	5-25µg/ml
	Regression Coefficient	$R^2 = 0.999$
	Regressed line equation (y = mx + c)	y = 0.025x + 0.008

Where y is the response, x is the concentration, m is the slope and c is the intercept of a best fit line to the data.

Drug-Excipient compatibility study by FT-IR

FT-IR spectra of drug and drug + excipients are shown in Figure 5. The presence of characteristic peaks associated with specific structural characteristics of the drug molecule was noted. Various peaks of the drug are shown in Figure 5. The appearance or disappearance of peaks and/or the shift of their positions are often indications of interactions such as hydrogen bonding. Terbutaline sulphate presented characteristic peak at 3373.61 cm^{-1} due to NH stretching 3610.00cm^{-1} was due to OH stretching vibration. At 1483.31cm^{-1} presenting C=C stretching vibration peak.

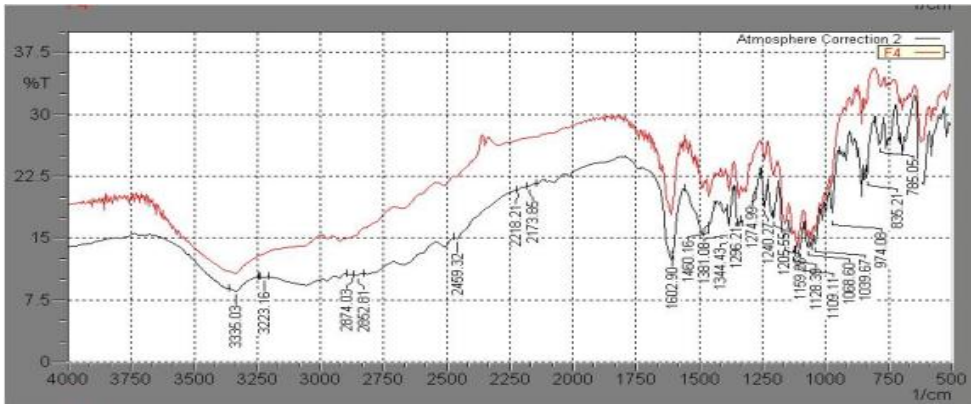

Figure 5: FT-IR overlay spectra of drug and drug +excipients

When the data obtained from FTIR spectra is compared with the standard spectra it was observed that there are similar peaks for functional groups in terbutaline sulphate, this shows there is no interaction/ incompatibility between terbutaline sulphate and excipients.

Evaluation of Fast Dissolving Oral Films

Table 4: Evaluation of formulations prepared using 2^3 factorial designs

Formulation	Disintegration time (sec)	Tensile strength (Mpa)	Elongation (%)	Folding endurance (nos.)	$CPR_{1\ min}$	$CPR_{10\ min}$
F1	33.91±0.12	4.29±0.15	23.17±0.14	187±2.0	21.32±1.25	50.34±1.56
F2	18.90±0.15	1.71±0.12	14.62±0.15	148±5.0	29.69±2.15	68.13±2.56
F3	34.50±0.23	2.47±0.15	20.23±0.11	161±3.0	22.54±3.15	56.39±3.15
F4	33.90±0.14	4.28±0.12	26.78±0.12	193±4.0	23.97±4.14	60.08±3.45
F5	26.70±0.15	2.83±0.11	20.21±0.14	179±5.0	30.18±3.15	71.46±2.15
F6	19.90±0.42	2.95±0.09	18.95±0.12	153±7.0	35.16±4.56	80.29±4.15
F7	23.80±0.36	3.59±0.15	23.81±0.11	203±2.0	32.13±2.25	76.10±2.52
F8	24.90±0.14	2.71±0.21	24.13±0.08	166±4.0	28.25±4.25	64.37±3.25

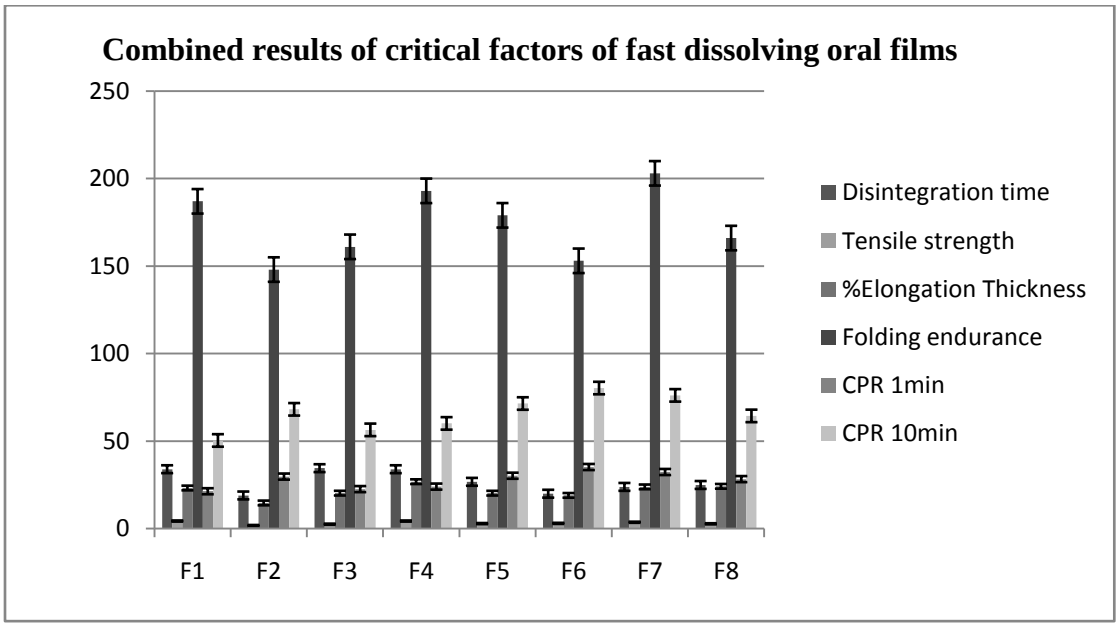

Figure 6: Graph for comparative evaluation of critical responses

Table 5: *In-vitro* drug dissolution showing CPR of film formulations F1-F8

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8
0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1	21.32±1.25	29.69±2.15	22.54±3.15	23.97±4.14	30.18±3.15	35.16±4.56	32.31±2.25	28.25±4.25
2	23.46±1.98	32.56±0.85	25.21±1.46	26.89±1.38	38.41±1.31	41.74±1.55	35.77±1.34	31.95±1.25
3	27.45±1.56	35.74±1.57	31.65±1.73	32.94±0.96	43.23±1.42	46.39±1.42	38.67±1.45	35.63±1.81
4	30.75±0.84	39.48±1.36	33.58±1.24	38.35±1.65	45.27±1.53	52.59±0.94	42.96±1.36	38.45±1.65
5	32.19±1.39	41.73±0.97	37.57±0.72	42.06±1.94	48.69±1.25	57.28±1.56	49.69±1.93	45.35±1.44
6	34.75±1.92	43.59± 1.53	45.03±1.45	46.57±1.66	53.59±0.96	64.29±0.87	53.62±1.42	51.58±1.73
7	36.59±0.93	48.09±0.85	48.18±1.62	49.86±1.51	59.92±1.43	68.56±1.63	57.19±0.85	53.96±0.89
8	46.02±1.05	57.21±1.94	51.57±1.72	53.03±1.05	62.67±1.73	73.23±1.06	65.03±1.48	57.98±1.93
9	49.45±1.81	61.58±1.63	53.49±0.89	58.46±0.93	67.03±1.56	75.04±1.91	71.46±1.39	62.77±1.45
10	50.34±1.56	68.13±2.56	56.39±3.15	60.08±3.45	71.46±2.15	80.29±4.15	76.10±2.52	64.37±3.25

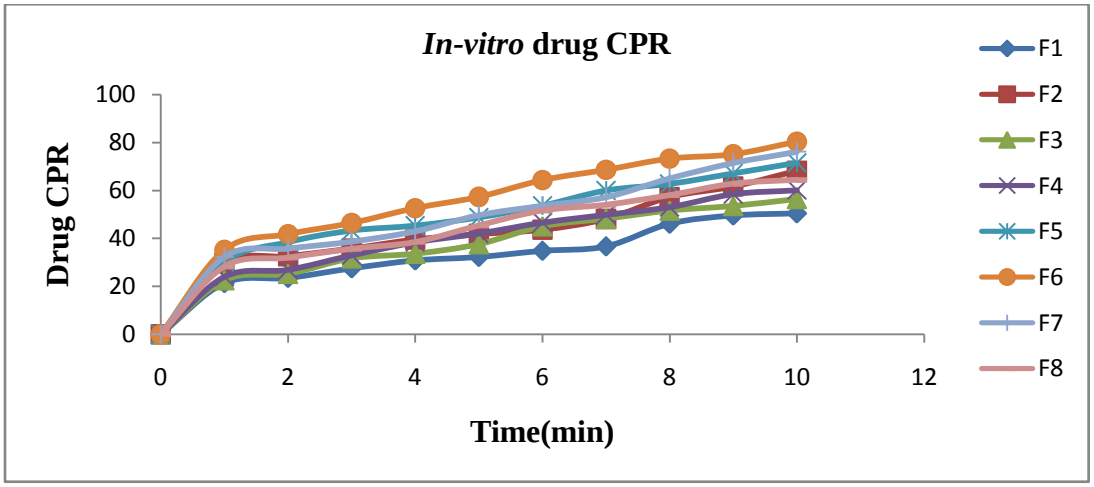

Figure 7: In-vitro drug dissolution showing CPR of formulations F1-F8

Table 6: Summary of ANOVA applied to 2^3 factorial designs responses

Factor	Disintegration Time		%Elongation		Folding Endurance		CPR 10min	
	Coeff.	P Value	Coeff.	P Value	Coeff.	P Value	Coeff.	P Value
Intercept	+27.06	0.0285	+21.49	0.0018	+173.75	0.0127	+65.90	0.0025
X1	+2.51	0.0757	+2.00	0.0030	+16.75	0.0033	-1.40	0.1971
X2	-4.74	0.0109	-2.09	0.0026	-3.00	0.3249	+8.10	0.0009
X3	-1.44	0.2441	+1.93	0.0035	+5.00	0.1350	+4.32	0.0089
r^2	0.8740		0.9687		0.9166		0.9633	
Adj r^2	0.7795		0.9453		0.8540		0.9358	
F	9.25		41.30		14.65		35.02	
P	0.0285		0.0018		0.0127		0.0025	

Table shows the results obtained from design for various response variables. Implementation of design helped in identifying the most significant factors for further detailed investigation with minimum experimentation thus saving considerable time, efforts and resources.

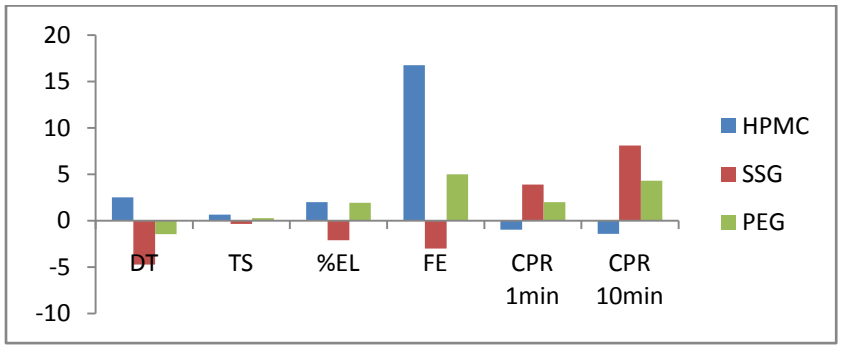

Figure 8: Results of design for selected response variables

Graph shows that HPMC K15LV and sodium starch glycolate has more effect on response variables compared to PEG-400, in the formulation of fast dissolving oral films. So, amount of HPMC E15LV and sodium starch glycolate were selected for further studies.

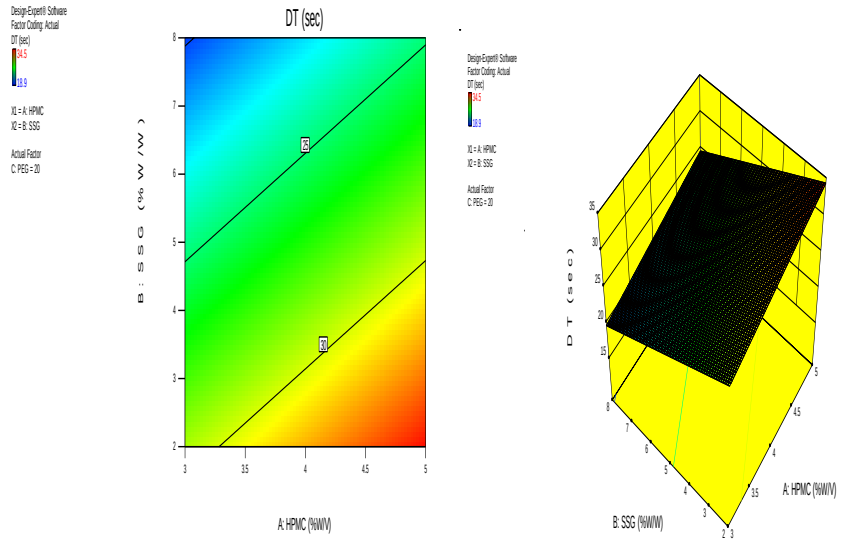

Figure 9: Contour Plot and response surface plot for D.T.

Disintegration Time: From contour plots and surface plots it can be observed that disintegration time of fast dissolving oral films increases with increase in concentration of HPMC E15 LV whereas it decreases with increase in concentration of sodium starch glycolate, which confirms with the literature as large concentration of polymer in films increases time for absorption of saliva which is due to its high viscosity and formation of jelly like mass whereas sodium starch glycolate absorbs saliva rapidly and swells to disintegrate films

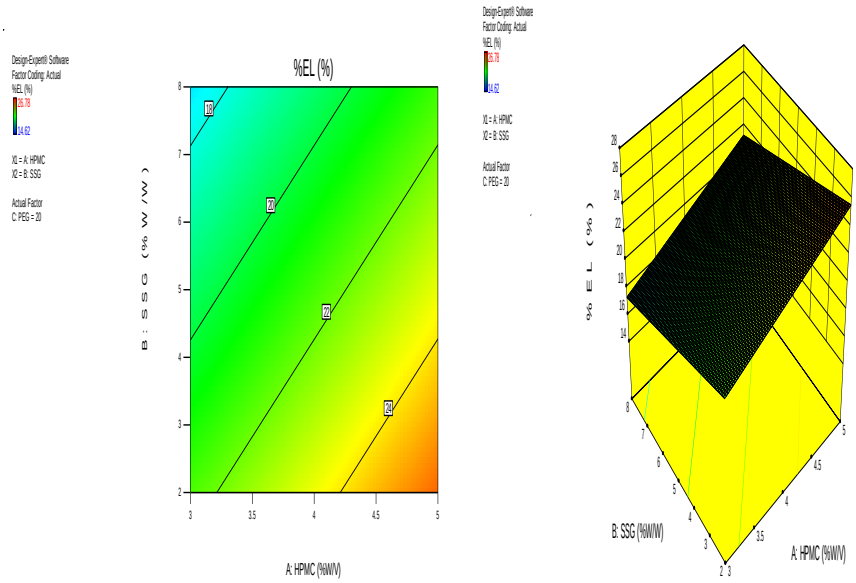

Figure 10: Contour plot and response surface plot for % Elongation

Percent elongation: From contour plots and surface plots it can be observed that percent elongation of fast dissolving oral films increases with increase in concentration of HPMC E15 LV whereas it decreases with increase in concentration of sodium starch glycolate, which confirms with the literature as large concentration of polymer in films increases its strength and stretch ability whereas sodium starch glycolate increases brittleness and porosity thereby reducing percent elongation.

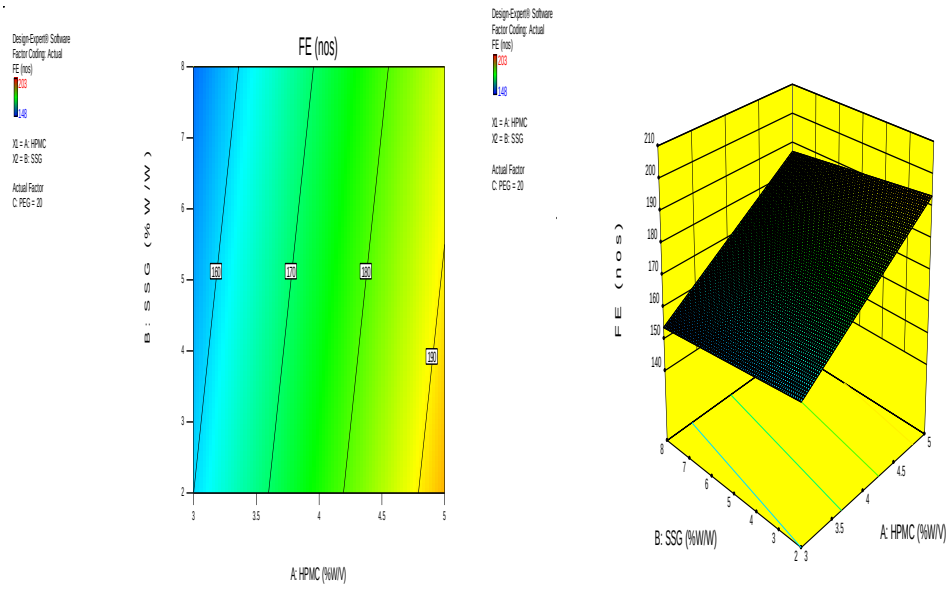

Figure 11: Contour plot and response surface plot for Folding Endurance

Folding endurance: From contour plots and surface plots it can be observed that folding endurance of fast dissolving oral films increases with increase in concentration of HPMC E15 LV whereas it decreases with increase in concentration of sodium starch glycolate, which confirms as expected, as large concentration of polymer in films increases its strength and flexibility whereas sodium starch glycolate increases brittleness and porosity thereby reducing folding endurance.

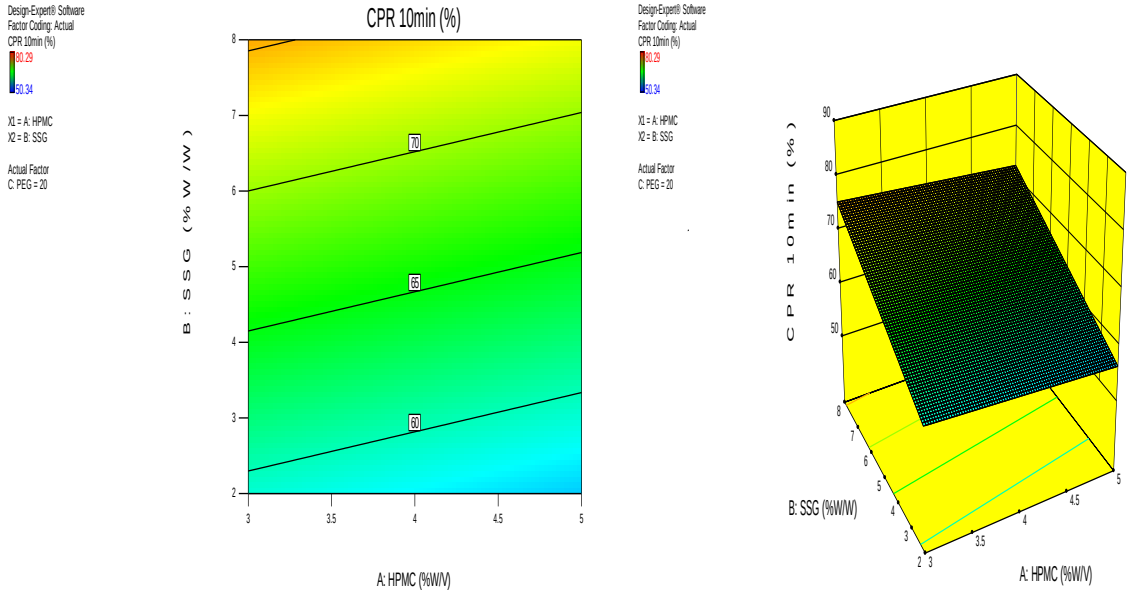

Figure 12: Contour plot and response surface plot for CPR 10_{min}

Cumulative percent drug release: From contour plots and surface plots it can be observed that disintegration time of fast dissolving oral films increases with increase in concentration of HPMC E15 LV, thereby reducing cumulative percent drug release. Whereas CPR increases with increase in concentration of sodium starch glycolate, which confirms with the literature as large concentration of polymer in films increases time for absorption of saliva which is due to its high viscosity and formation of jelly like mass whereas sodium starch glycolate absorbs saliva rapidly and swells to disintegrate films and thereby increases CPR.

Conclusion

The formulated films of terbutaline sulphate were evaluated for their physico-mechanical parameters like thickness, disintegration time, tensile strength, folding endurance, thickness, disintegration time and *In-vitro* drug release. Estimation of drug content uniformity of terbutaline sulphate films was performed and the results were satisfactory. The prepared fast dissolving oral films of terbutaline sulphate were evaluated and all films were found to be smooth and elegant with uniform distribution of drug, the thickness of films was found in the range of 0.174± 0.008 to 0.264±0.005 mm, disintegration time of 18.90±0.15 to 39.344 ±0.409sec, drug content of 97.466±0.53-82.488±1.891%, tensile strength of 4.29±0.015-1.71±0.12 Mpa, percent elongation of 14.62±0.15 to 26.78±0.12and folding endurance of 148±5.0-203±2.0. The optimized batch F6 showed maximum drug release of 80.29±4.15 in 10 minutes with thickness of 0.254± 0.01mm, disintegration time of 19.90±0.42 seconds, tensile strength of 2.95±0.09Mpa, % elongation of 18.95±0.12 and folding endurance of 153 ± 7.0.

Data from ANOVA model from Design Expert® software 10 trial version shows that for disintegration time r^2 value was found to 0.8740, F value of 9.25 and P value 0.0285 indicates that model is significant. For percent elongation r^2 value was found to 0.9687, F value of 41.30 and P value indicates that model is significant. For folding endurance r^2 value was 0.9166, F value is 14.65 and P value is 0.0127.Cumulative percent release at 10 minutes shows values of r^2 as 0.9633, F value of 35.02 and P value of model as 0.0025. As for all models r^2 values are near to 1, F calculated

values more than critical F values and P values less than 0.05.This signifies that applied models are significant at 5% levels.

Response surface plot and contour plot also gave the idea about how HPMC E15 LV and SSG concentration affects the results of fast dissolving oral film.It was concluded that HPMC E15LV is a good film forming polymer and SSG in high concentration and PEG in medium range gives films fastest drug release. Faster action was desired in case of asthma like emergency life threatening medical condition and that was achieved by only and only if drug terbutaline sulphate goes immediately into the systemic circulation by bypassing the first pass effect (shorter T_{max}) after administration of dosage form.

Fast dissolving oral film of terbutaline sulphate was successfully developed with good *In vitro* and *In vivo* characteristics at laboratory scale. Hence, developed fast dissolving oral film formulation of terbutaline sulphate can bring a new era of drug delivery in future for treatment of asthma in pediatric and geriatric patients or patients who are travelling.

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Conflict OF INTERESTS

The authors report no conflict of interests.

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