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Development and Optimization of Oral Fast Dissolving Film of Salbutamol Sulphate by Design of Experiment

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ABSTRACT

The present study aimed at development and evaluation oral fast dissolving film of Salbutamol Sulphate utilizing HPMC as a film forming polymer and PEG 1000 as a plasticizer. Response Surface Methodology was used to optimize the oral fast dissolving film formulation. In the design, concentration of HPMC and concentration of PEG 1000 was selected as independent variable. Tensile strength, elongation at break and elastic modulas was selected as dependent variable. The results of the study demonstrated a successful development of a film with optimum mechanical property and disintegration time. The adopted design was very much successful as an optimization tool in this present study. The optimized formulation was evaluated by SEM & FTIR and the results were found appropriate. The accelerated stability study indicated the stability of the optimized formulation up to 6 month. In the conclusion, it is advocated that the development of optimized oral fast dissolving film formulation was successful.

Key words: Plasticizer, Oral Fast Dissolving Film, Factorial Design, Elongation at break

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INTRODUCTION

Asthma is a chronic inflammatory disease, which includes bronchial hyperactivity and bronchospasm characterized by hyper responsiveness of tracheo-brochial smooth muscle to variety of stimuli , resulting in narrowing of air tubes, often accompanied by increased secretions and mucosal edema resulting in breathlessness or dyspnea, wheezing cough, chest congestion and anxiety about being unable to breathe. The treatment of asthmatic symptoms generally includes conventional oral dosage forms like tablets, capsules, oral liquids etc.; inhalation therapy includes metered dose inhalers with or without spacers, dry powder inhalers, and other aerosol systems, but conventional oral dosage forms are associated with lag time and delayed onset of action. Many geriatric and paediatric patients find it difficult to swallow solid dosage forms such as tablets or capsules T. Hanawa (1997). Aerosol systems are specific but fail to deliver the actual dose of drug with only ten percent of administered dose deposited on the bronchi while rest of the drug is deposited in oropharynx and is swallowed. Also, metered dose system are less potable while dry powder inhalers cause clogging of device and require skilful operation. Salbutamol sulphate, a selective β_2-adrenergic agonist and bronchodilator, is one of the widely used drugs for the treatment of the most respiratory diseases arising due to airway obstruction (1). It is a hydrophilic drug with a dissociation constant of (pKa) 9.2 and a log P value of 0.11(2).

Research and development in the oral drug delivery segment has led to transition of dosage forms from simple conventional tablets/capsule to oral disintegrating tablet to wafer to the recent development of oral fast dissolving film (OFDF). Basically the oral film can be considered as an ultra thin film of postage stamp size with an active pharmaceutical ingredient (API) and other excipients. The advantages of convenience of dosing and portability of OFDF have led to wider acceptability of these dosage form by paediatric as well as geriatric population equally (3-7). The advantages of OFDF include larger surface area that leads to rapid disintegrating & dissolution, flexible in handling & transportation, accuracy in the administered dose and consumer-friendly due to its ease of swallowing property(8). A fast dissolving film form would thus be advantageous, as salbutamol sulphate is water-soluble and its preparation into a fast dissolving form would render it to dissolve rapidly and thereby result in rapid absorption without any lag time.

Hydroxypropyl-methylcellulose (HPMC) is a hydrophilic polymer commonly used in fast dissolving film formulation.On another hand, the utilization of plasticizers is necessary to reduce brittleness of film (9-11).According to literature HPMC film are most effectively plasticized with polyethylene glycol (PEG)(12).

The factorial design used to find simultaneously the effect of the individual variables and their interactions at several levels with a minimum of experiments. Factorial experimental designs have been employed to optimize fast dissolving film of Domperidone(13), Ropinirole Hydrochloride (14), Levocetrizine Dihydrochloride (15)), Zolmitriptan (16) and Ondansetron Hydrochloride (17). The application of factorial experimental design has also been reported for fast dissolving film of salbutamol Sulphate containing polyvinyl alcohol as a polymer, glycerol as a plasticizer, and mannitol as filler(18).

The objective of this work was to study the mechanical properties and disintegration time of fast dissolving film of salbutamol sulphate formulate at various concentration of film forming polymer (HPMC) and plasticizer (PEG 1000) by using factorial design.

MATERIAL AND METHOD

Preparation of fast dissolving film

Hydroxy propyl methyl cellulose, PEG 1000 were passed through sieve no. 40 and mixed uniformly using geometrical dilution method. The powder blend was dissolved in 30 ml of distilled water and stir for 4 hr at 2000 rpm (Solution A). Saccharine sodium, Pineapple flavour and salbutamol sulphate were separately dissolved in 10 ml of distilled water (Solution B) and mixed to the solution prepared earlier. The volume was making up to 50 ml with distilled water and stir for 1 hr at 2000 rpm. This final solution was kept for 1 hr to remove all the entrapped air bubble and 5 ml of this solution was cast in to polypropylene petri plate. The petri plates were dried in a tray dryer at 60^0C for 6 hr. The film was removed from petri plate and stored in a desiccator(8, 18).

Factorial Design

In this work a 3^2 factorial design was used for the optimization of OFDF. The effect of two factors on the mechanical property of OFDF was studied at 3 levels. HPMC concentration and PEG 1000 concentration were selected as the independent variables whereas TS (tensile strength), EB (% elongation at break) and EM (Elastic Modulus) were selected as dependent variables. Different trial formulations of OFDF were prepared according to the trial proposal of 3^2 factorial designs. The prepared OFDF were evaluated for mechanical property. The responses were analyzed using ANOVA and the individual response parameters were evaluated using F test and polynomial equation was generated for each response using multiple linear regression analysis (MLRA). The study design including investigated factors and responses is shown in Table 1.

A suitable OFDF should have a moderate tensile strength, high % elongation and low elastic

modulus therefore the optimized formulation was prepared which have the TS in range 5.5-6.5 MPa, EB is maximize and EM is minimize(18). Constraints for responses and factors are shown in Table 2. By utilizing the software, we got one solution for optimized formulation. The optimized formulation is prepared and evaluated for TS, EB and EM. Observe response value of the optimized formulation is compared with predicted value. The optimised batch(s) was further investigated by DSC and FTIR.

Film thickness

The film thickness was measured using a micrometer (Mitutoyo,model 102-309, Tokyo, Japan) with an accuracy of ±1 µm. Each film sample was measured at random five positions (centre and four other positions along the strip).An average value was reported. The average thickness was used to calculate mechanical properties of each film sample.

Uniformity of dosage units of OFDF

Uniformity of dosage unit of OFDF was determined by assay of 20 units individually using UV spectrophotometric method and calculate acceptance value by using soft catalyst software (Aura health quest). The acceptance value (AV) of the preparation is less than 15%, according to the JP15. In USP30, the contents should be within a range between 85% and 115%, and the relative standard deviation should be less than or equal to 6.0% (19-21).

Film Flexibility

The film flexibility was measured using ASTM bend mandrel test method (D 4338 – 97). A 2 X 3 cm film was bended over a mandrel and observed for cracks in a strong light. The acceptance criteria for flexible was, no cracks was shown at 5x magnification (11, 22).

Surface pH measurement

The pH OFDF must be neutral, so that no irritation occurs after administration in oral mucosa . The surface pH of OFDF was determined according to method described by Bottenberg *et al.* OFDF were kept to swell on surface of agar plate (prepared by dissolving 2% agar in warmed isotonic phosphate buffer (pH 6.8) under stirring and then pouring the solution into a Petri dish till it gelled at room temperature).The pH of OFDD was assessed by getting the electrode in contact with surface of OFDF, letting it to equilibrate for 5 min. The measurement of pH was replicated three times (2, 23).

Mechanical properties

The mechanical properties of OFDF were determined by ASTM International Test Method for Thin Plastic Sheeting (D 882-02), with an TA.XT2 texture analyzer equipment equipped with a 5 kg load cell (Stable Micro Systems,Haslemere, Surrey, UK).The film was cut in to 50 mm

x10mm strip and equilibrated at 25^0C for one week.Each OFDF strips were held in tensile grips of texture analyzer positioned at a distance of 30 mm . The crosshead speed was 500 mm/min. The test was considered over at the film break. The tensile strength (force/initial cross-sectional area) and elongation at break ($\Delta l/l_0$) were determined directly using the software Texture Expert V.1.15 (SMS) from the stress x strain curves, and the elastic modulus was calculated as the slope of the linear initial portion of this curve (22, 24, 25).

***In Vitro* disintegration study**

Disintegration of fast disintegrating preparation *in vivo* is attained by saliva, however amount of saliva in the mouth is limited and official disintegration test was not correlate with in vivo conditions. A modified method actually reported by Fu et al.(2006) for fast disintegrating tablet was used to determine disintegration time of the OFDF. A cylindrical vessel was used in which 10-mesh screen was placed in such way that only 2 ml of disintegrating or dissolution medium would be placed below the sieve. To ascertain disintegration time, 3 ml of Sorenson's buffer (pH 6.8), was placed inside the vessel. The OFDD was kept on sieve and whole assembly was shook. The disintegration time is the time when all the particles pass through the sieve (26, 27).

***In vitro* dissolution study**

The *in vitro* drug dissolution study was carried out in 100 mL of Sorenson's buffer (pH 6.8) at 37.0±0.5°C, using USP 23 type 2 paddle method (Electrolab, EDT-08Lx) at a stirring speed of 50 rpm. The OFDF of 6 cm^2 was fixed on the glass disk with the help of a cyanoacrylate adhesive. The disk was put at the bottom of the dissolution vessel so that the OFDF remained on the upper side of the disk. 3 mL of samples were withdrawn at predetermined interval (1,2, 3,4, 5, 10, 20 and 30 min) and replaced with fresh medium. The samples were filtered through 0.45 µm filter and appropriately diluted with Sorenson's buffer (pH 6.8) and assayed spectrophotometrically at 278 nm **(2)**.

Stability study

Optimized OFDF formulation was wrapped in butter paper followed aluminium foil and was stored at 40^0C/75 % RH for 6 month. The OFDF was evaluated for flexibility, surface pH, mechanical strength and disintegration time after 1,2,3 and 6 month.

Fourier Transform Infrared Spectroscopy

Drug and excipients compatibility was evaluated by Fourier transform infrared (FTIR) spectroscopy (840, Shimadzu, Japan) of pure drug and optimize formulation (OFDF 10).The pellets of sample and potassium bromide were prepared by compressing at 20 psi on hydraulic press and spectra range was 4000-600 cm^{-1}. Each spectrum was acquired by performing 32 scans.

RESULT AND DISCUSSION

Formulation Design

Solvent casting method was used because of its ease of manufacture and lower cost (3). In our previous work, the ability of PEG 1000 as an effective plasticizer to formulate oral fast dissolving film (OFDF) of Salbutamol sulphate prepared by the solvent lasting method was demonstrated.PEG 1000 reduces the glass transition temperature (Tg) of HPMC and thus increase the elasticity of OFDF formulation. Hence, concentration of plasticizer was selected as one of the independent variable for experimental design. HPMC a film forming agent was selected as another variable as it may affect the mechanical properties & disintegration time of the OFDF formulations.

Tensile strength of the formulation obtained of all the experimental run had a range of 4.96 – 7.21 Mpa, Elongation at break (%) had a range of 106 – 301 %. Elastic modular was found in range 0.34 – 2.1Mpa. The observation show that mechanical property of film strongly depends upon the selected independent variables. The model (full and reduced) relating the response TS, EB(%) and EM are shown in table1. Analysis of variance (ANOVA) indicated that assumed regression models were significant and valid for each of the response (P <0.05) (Table 3& 4).

Table 1. Factorial design layout.

Formulation	Variables in coded Form		TS	EB	EM
	X1(%)	X2(%)			
OFDF 1	-1	-1	5.96	106	2.1
OFDF 2	0	-1	6.75	156	1.8
OFDF 3	1	-1	7.21	197	1.4
OFDF 4	-1	0	5.37	183	1.1
OFDF 5	0	0	6.19	206	0.9
OFDF 6	1	0	6.43	238	0.7
OFDF 7	-1	1	4.96	242	0.56
OFDF 8	0	1	5.65	279	0.4
OFDF 9	1	1	5.87	301	0.34
OFDF 10	**19.85**	**29.80**	**5.88**	**304.44**	**0.34**

Coded Value	Actual Value (%)	
	X1	X2
-1.000	**10.00**	**10.00**
0.000	**15.00**	**20.00**
1.000	**20.00**	**30.00**

X1 indicates amount of HPMC (%); X2, amount of PEG 100 (%w/w of HPMC); TS,Tensile strengthMpa();EB, Elongation at break(%) and EM (MPa) Elastic modulus. OFDF 10 used as checks point and optimized batch.

Table 3. Summary of results of regression analysis.

For TS						
Response	**b_0**	**b_1**	**b_2**	**b_{12}**	**b_{11}**	**b_{22}**
FM	6.15	0.54	– 0.57	– 0.085	– 0.23	0.070
P value	-	< 0.0001	< 0.0001	0.0277	0.0046	0.100
RM	6.20	0.54	-0.57	– 0.085	– 0.23	-
P value	-	< 0.0001	< 0.0001	0.0508	0.0602	-
For Q_{45}						
FM	210.67	34.17	60.50	-8.00	-2.50	4.50
P value	-	0.0018	0.0003	0.1346	0.6834	0.4774
RM	212	34.17	60.50	-	-	-
P value	-	< 0.0001	< 0.0001	-	-	-
For Q_{10}						
Response	**b_0**	**b_1**	**b_2**	**b_{12}**	**b_{11}**	**b_{22}**
FM	0.90	– 0.22	– 0.67	0.12	0.1	0.20
P value	-	0.002	0.0008	0.001	1.00	0.0054
RM	0.90	– 0.22	– 0.67	0.12	-	0.20
P value	-	< 0.0001	< 0.0001	0.0020	-	0.0011

FM indicates Full model and RM, Reduce Model.

Table 4. Result of Analysis of variance (ANOVA)

For TS					
Regression	**Df**	**SS**	**MS**	**F**	**R^2**
FM	5	3.84	0.77	429.86	0.9986
RM	4	3.84	0.96	252.86	0.9961
Residual					
FM	3	5.36×10^{-3}	1.78×10^{-3}		
RM	4	0.015	3.79×10^{-3}		
For EB					
FM	5	29274.67	5854.93	94.77	0.9937
RM	2	28965.67	14482.83	175.79	0.9832
Residual					
FM	3	185.33	61.78		
RM	6	494.33	82.39		
EM					
FM	5	3.09	0.62	409.59	0.9985
RM	4	3.09	0.77	682.65	0.9985
Residual					
FM	3	4.53×10^{-3}	1.51×10^{-3}		
RM	4	4.53×10^{-3}	1.13×10^{-3}		

DF indicates: degrees of freedom; SS, sum of squares; MS, mean of squares; F, ischer's ratio; R^2, regression coefficient.

Multiple linear regression analysis

The mathematical relationship generated using multiple linear regression analysis for the variables all shown in table 3. Model reduction was carried out by excluding nonsignificant terms ($P > 0.05$) in model equations resulting from the multiple regression analysis. The polynomial equation for each response variable were as follow.

$$TS = 6.15 + 0.54\ X_1 - 0.57X_2 - 0.085\ X_1X_2 - 0.23\ X_1^2$$

$$EB = 212 + 34.17\ X_1 + 60.50X_2$$

$$EM = 0.90 - 0.22\ X_1 - 0.67X_2 + 0.12\ X_1X_2 + 0.20X_2^2$$

The polynomial equation for tensile strengths showed good correlation coefficient (0.9979). Result of multiple linear regression analysis indicate (Table 3) that X_1 (HPMC Concentration& X_2 (PEG 1000 concentration) have significant effect on tensile strength. Moreover, PEG 1000 concentration had a negative effect on the tensile strength, coefficient of X_2 bear negative sign. As the PEG 1000 concentration increases, the tensile strength (TS) of formulation was decreased resulting in a fragile film. An increase in concentration of film forming agent (HPMC) leads to an increase in tensile strength because the coefficient b_1, bear a positive sign. The three dimensional response surface plot and corresponding contour plot (Fig.1) indicate the positive and negative effect of HPMC concentration (X_1) & PEG 1000 on the tensile strength (TS) respectively.

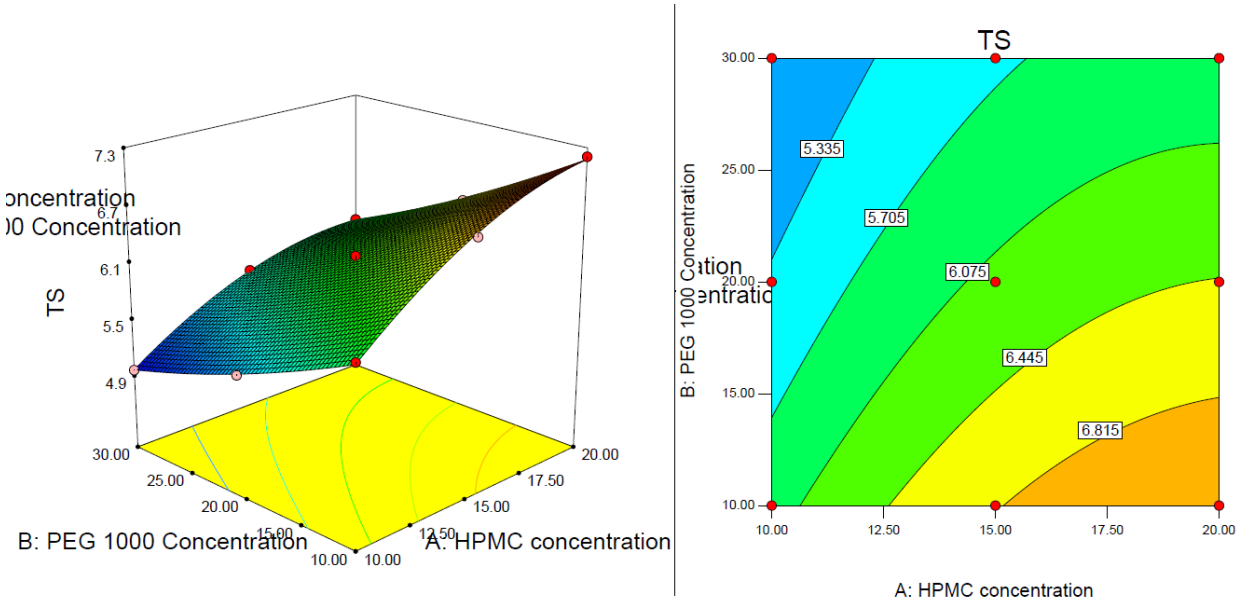

Figure 1: Response surface plot showing the influence of HPMC concentration and PEG concentration on TS (Mpa) and corresponding contour plot showing the relationship between various levels of 2 independent variables.

The elongation at break (EB) is an important variable for assessing ductility/flexibility of film formulation. The elongation at break showed good correlation coefficient (0.9832). Result of multiple regression analysis indicates that X_1 (HPMC concentration) & X_2 (PEG 1000 concentration) have positive effect on EB (%), both the coefficient b_1 and b_2 bear a positive sign. The three dimensional response surface plot & corresponding contour plots (Fig.2) indicate that increased value of EB with the increment of both independent variables (HPMC concentration and PEG 1000 concentration).

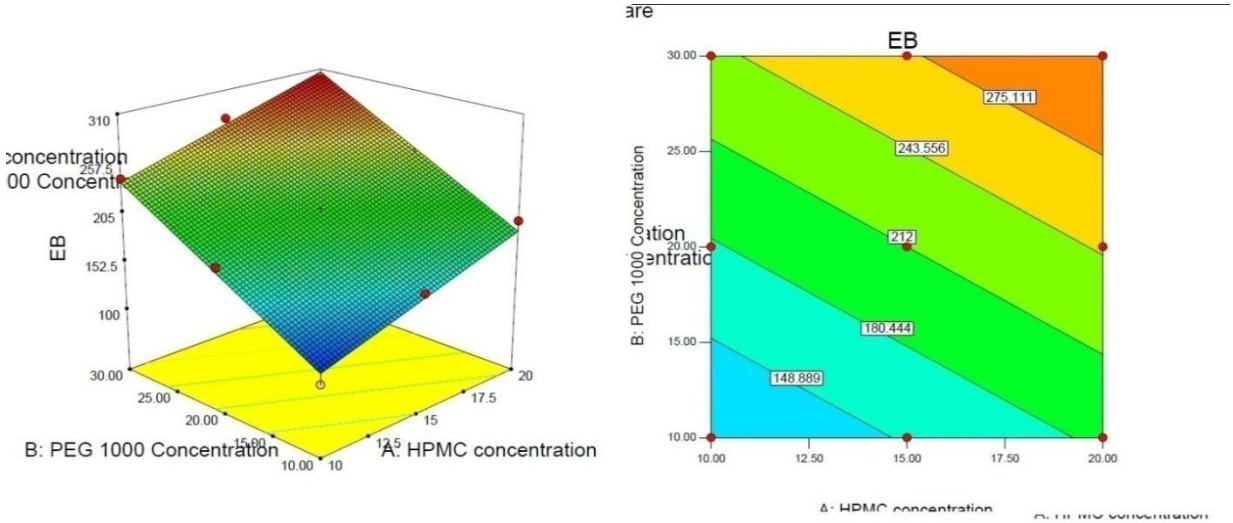

Figure 2: Response surface plot showing the influence of HPMC concentration and PEG concentration on EB (%) and corresponding contour plot showing the relationship between various levels of 2 independent variables.

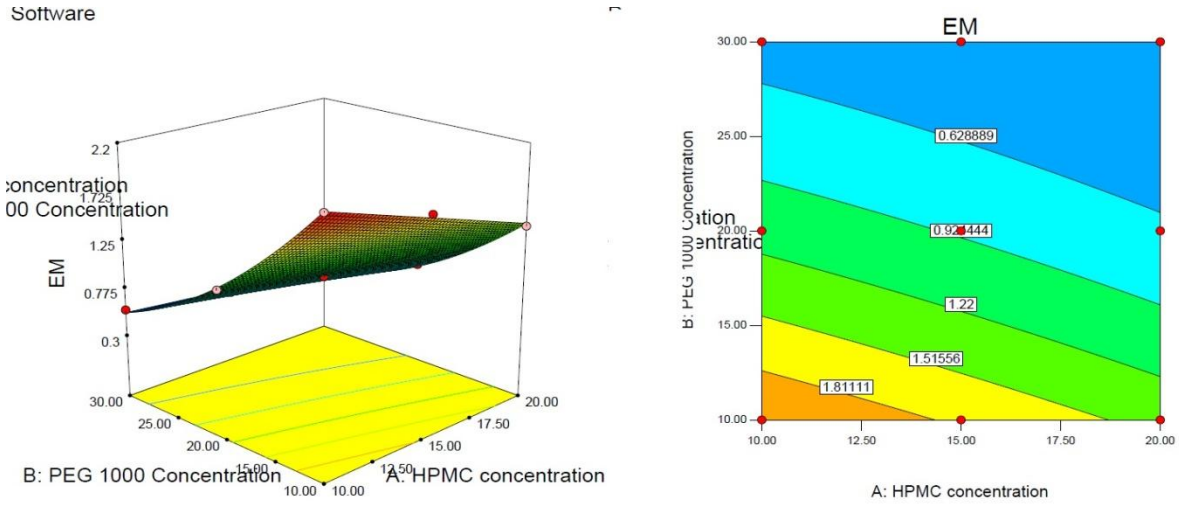

Figure 3: Response surface plot showing the influence of HPMC concentration and PEG concentration on EM (Mpa) and corresponding contour plot showing the relationship between various levels of 2 independent variables.

Elastic modulus is an indicator of stiffness and tensile stress of film formulation. The result of multiple regression analysis shown that both independent factor X_1 & X_2 have negative effect on EM, both the coefficient b_1 and b_2 bear a negative sign. The three dimensional response plot & corresponding contour plots (Fig.3) also exhibit that elastic modulus vary in descending pattern with an increase in both variable.

To validate the model a numerical optimization technique based on the desirability approach was adopted. A optimize formulation (OFDF 10) was selected based on the criteria a fast dissolving film have moderate TS, High EB & Low EM. The independent variable X_1 (HPMC concentration) and X_2 (PEG 1000 concentration) for formulation of optimize OFDF formulation (OFDF 10) were 19.85% & 29.80% respectively (Table 1&2). The observed value of TS, EB, & EM of check point batch/optimize formulation (OFDF 10) were in close agreement with the value predicated by model (Fig.4). Thus we can conclude that the statically model was valid.

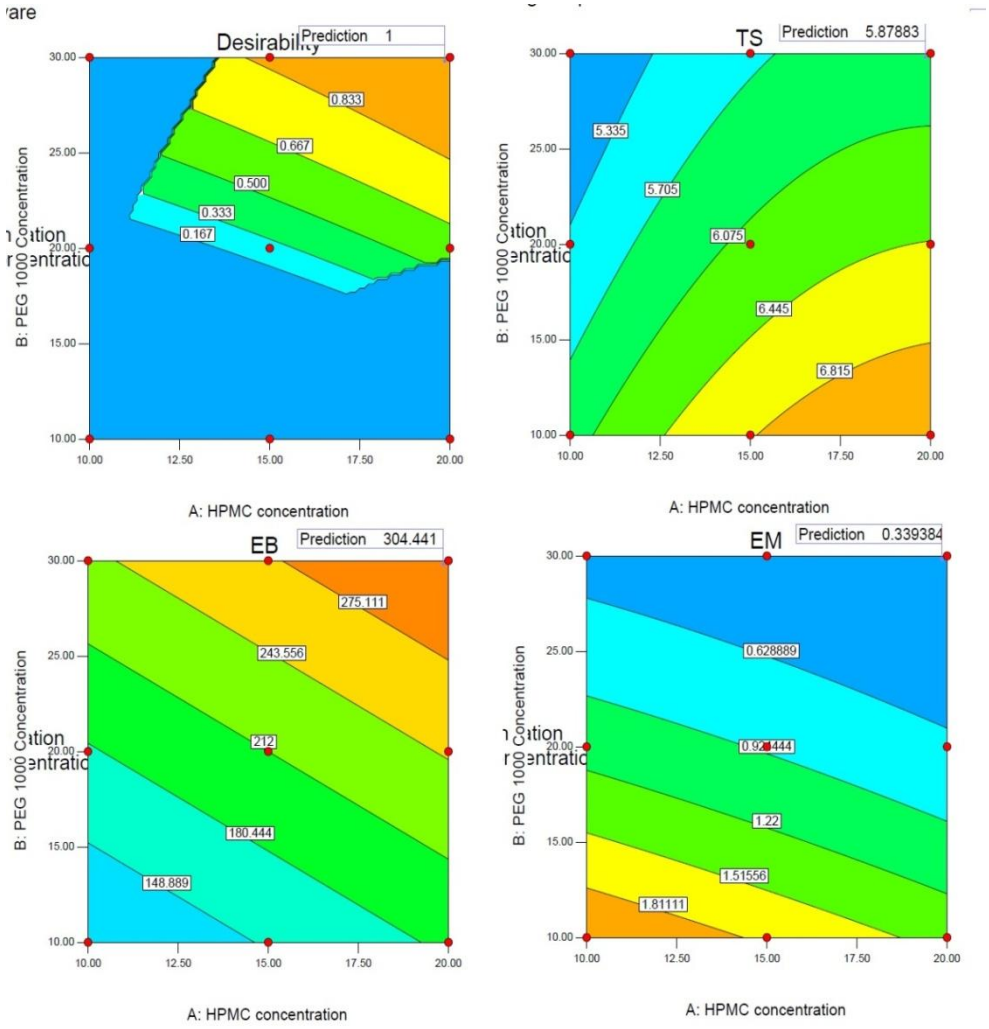

Figure 4: Response surface predication plot Desirability, TS, EB and EM.

Table 2. Optimization of OFDF formulation.

Constraints			
Name	**Goal**	**Lower limit**	**Upper Limit**
HPMC concentration	In range	10	20
PEG1000 concentration	In range	10	30
TS (Mpa)	In range	5.5	6.5
EB (%)	maximize	106	301
EM (Mpa)	minimize	0.34	1.0

SOLUTION (OFDF 10)					
HPMC concentration	**PEG 1000 concentration**	**TS**	**EB**	**EM**	**Desirability**
19.85	**29.80**	**5.88**	**304.44**	**0.34**	**1.00**

TS,Tensile strengthMpa();EB, Elongation at break(%) and EM (MPa) Elastic modulus. OFDF 10 used as checks point and optimized batch.

Effect of plasticizer concentration on mechanical property of film

Analyzing the effect of PEG 1000 used on plasticizer on mechanical property of film formulation, it can be observed that on increase in its concentration caused a reduction in the resistance (decrease in TS), stiffness & tensile stress (decrease in EM) and increase in ductility & flexibility (increase EB). This is due to increase in molecular mobility with the increase in PEG 1000 concentration similar plasticization effect can be observed by Maria et al (2008) and Chiellini et al (2001 a) .

Effect of HPMC concentration on mechanical property of film

The mechanical property result indicate that on increasing the concentration of HPMC, rigidity decreases (EM decrease), Increase in Mechanical resistance to break (TS increase) & increase in flexibility (increase in FB). OFDF containing high HPMC concentration is less prone to break, essay to handle & more durable compared to a OFDF containing less HPMC concentration.

Film thickness

The mean thicknesses of the OFDF formulations were 0.34 – 0.42 mm There was no stastically significant difference ($P > 0.05$) in thickness among the OFDF formulation (Table 5).

Uniformity of dosage unit

The average of salbutamol sulphate content in OFDF formulation ranged from 91.456 – 98.72%, with relative standard deviation (RSD) ranged from 0.43 – 1.34 %. Thus the OFDF formulations compile with the acceptance criteria of USP 32 content uniformity. Moreover acceptance value(AV) of OFDF ranged from 1.03 – 10, a value that was within the limit of (For L1, AV ≤ 15) of uniformity of dosage unit for JP 15.

Film Flexibility determination

The result of the film flexibility study showed no cracks after bended over a mandrel at a 5 x

magnification in a strong light. The flexibility of film is also indicated by result of mechanical property test.

Surface pH

The pH of OFDF formulations (Table 5) were found to be within the range 6.8-7.3, which is within the limit. The almost neutral pH reflected, the OFDF will be non-irritant to oral mucosa.

Table 5 Evaluation of OFDF formulations

Formulation	pH	Thickness	Disintegration Time (in second)	Uniformity		
				Drug Content	RSD	AV
OFDF1	6.8 ±0.08	0.34 ±0.01	27 ±0.61	92.684±0.97	1.04	8.32
OFDF2	7.1±0.12	0.37 ±0.01	24 ±1.23	91.456±1.23	1.34	10.0
OFDF3	7.2±0.14	0.41±0.08	26± 0.81	92.712±0.84	0.96	7.8
OFDF4	7.3±0.17	0.35 ±0.02	21± 0.72	97.280±0.98	1.00	3.57
OFDF5	7.3±0.18	0.38 ±0.05	23±0.65	97.650±1.32	1.35	4.01
OFDF6	6.9±0.21	0.40 ±0.06	25±0.90	97.28±0.56	0.57	2.564
OFDF7	7.2±0.18	0.36 ±0.08	20±0.87	98.52±0.76	0.77	1.824
OFDF8	7.1±0.12	0.38 ±0.05	24±0.57	95.84±0.48	0.50	3.812
OFDF9	6.9±0.21	0.42±0.06	23±0.62	98.72±0.43	0.43	1.03
OFDF10	7.2±0.21	0.39 ±0.04	23±0.82	94.23±0.64	0.67	5.81

RSD indicates: relative standard deviation; AV, Acceptance value.

In vitro disintegration study

The mean disintegration time of OFDF formulation were with the range 20-27 sec, which is met with acceptable criteria for disintegration test of oral dissolve formulation (within 30 minutes).

Dissolution of film formulation

Dissolution test was performed using Sorenson's buffer (pH 6.8). As shown in figure 5 all OFDF formulation were shown rapid dissolution, in which approximately 60.23 – 94.36 % drug release with in 5 minute. Liu et al and Mura et al had used polyethylene glycol as solubility enhancer in preparation of solid dispersion for dissolution enhancement of poorly water soluble drug. Moreover Chambin et al had shown that addition of HPMC brings out the steady dissolution. Therefore rapid dissolution of OFDF formulation may be due to presence of high amount of PEG 1000.

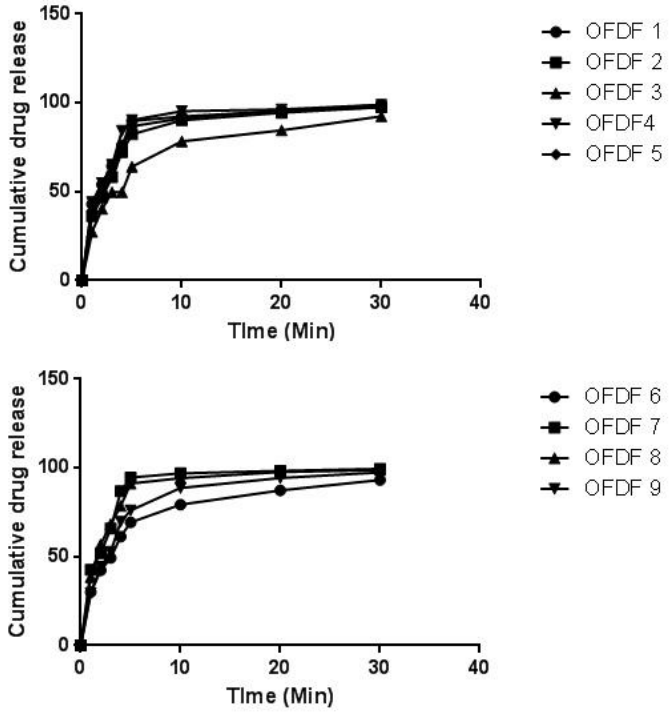

Figure 5: Dissolution profile of OFDF formulations.

Stability study

As shown in table 6, when the OFDF 10 was stored in accelerated stability study condition (40^0C ± 2^0C/75% ± 5% RH) for 6 months, no change in appearance and flexibility was observed. There was also no significant difference in mechanical property, surface pH and disintegration time of OFDF 10 after storage at accelerated stability study condition for 6 month.

Table 6 Accelerated stability (Temperature: 40^0C ± 2^0C, relative humidity: 75% ± 5%) of OFDF 10 formulation.

Parameter		Initial	Duration in Month		
			1	2	6
Description		Colourless, transparent and soft	Colourless, transparent and soft	Colourless, transparent and soft	Colourless, transparent and soft
Flexibility		No crack	No crack	No crack	No crack
Surface pH		7.2±0.21	7.2±0.26	7.3±0.31	7.3±0.61
Mechanical Properties	TS	5.88	5.85	5.82	5.80
	EB	304.44	303.34	301.28	299.35
	EM	0.34	0.34	0.35	0.36
Disintegration Time		23±0.82	23±0.81	24±0.61	24.5±0.45

TS,Tensile strengthMpa();EB, Elongation at break(%) and EM (MPa) Elastic modulus.

Fourier Transform Infrared Spectroscopy

While designing fast dissolving film, it was imperative to give consideration to the compatibility of salbutamol sulphate and excipients used within the systems. It was therefore necessary to confirm the interaction between excipients and drug. The FTIR spectra of salbutamol sulphate, and OFDF 10 are shown in fig 6**.** No interaction was seen between salbutamol sulphate and excipients.

Scanning Electron Microscopy

Morphology of OFDF 10 was characterized by SEM as shown in fig 7. OFDF 10 was homogenous with rough surface, which may be due to the presence of drug on surface.

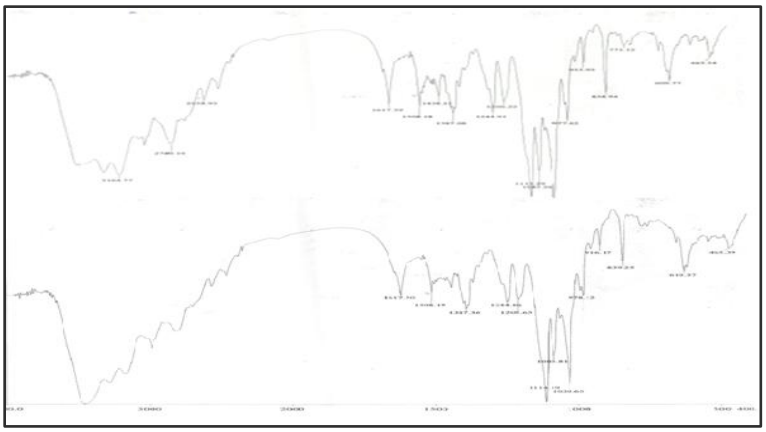

Figure 6: FTIR spectrum of salbutamol sulphate (a) and formulation (OFDF 10).

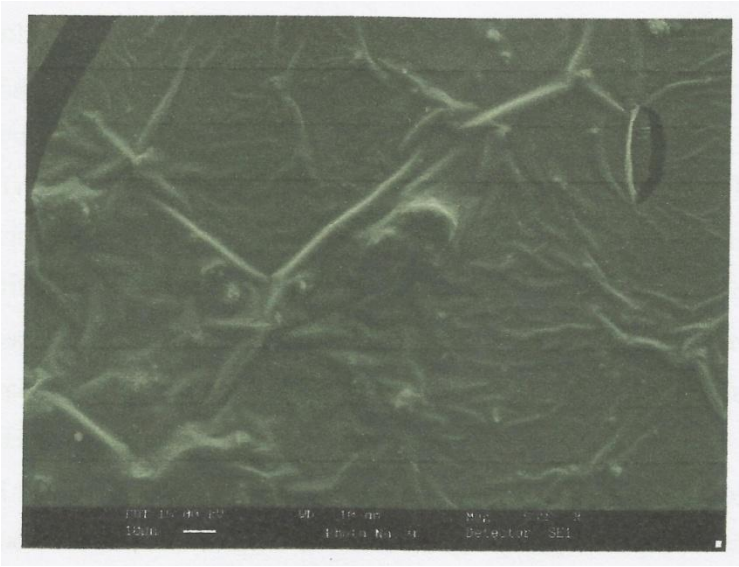

Figure 7: Scanning electronic microscopy of OFDF 10.

CONCLUSION

A flexible salbutamol sulphate ODDF formulation with rapid disintegration, acceptable mechanical property and stable over a period of 6 months was successfully developed. The

findings suggest that salbutamol sulphate OFDF has the potential as an alternative dosage form in treating Asthma.

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