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Development of Fast Dissolving Sublingual Wafers by Using Film Former: Optimization and Characterization

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ABSTRACT

The aim of the present research work was to develop, optimize and evaluate fast dissolving sublingual wafer of Tamsulosin hydrochloride using film former by solvent casting technique to treat benign prostatic hyperplasia. The xanthan gum, a natural polymer along with cross carmellose sodium as a super disintegrant and polyethylene glycol 400 as a plasticizer were used for forming sublingual wafer. The prepared film was evaluated for mechanical properties like percent elongation and tensile strength, weight variation, thickness, disintegration time, drug content, pH, folding endurance and in vitro drug release. Formulations were optimized by 3^2 factorial design. Drug loaded sublingual wafers of size 2 cm × 1.5 cm exhibited folding endurance of 210 ± 0.547, disintegration time 20 ± 0.577 seconds, tensile strength 27.33 ± 0.325 dyne/cm^{2}and drug release of 101.88% at the end of 20 seconds. The optimized formulation of film was characterized by DSC and PXRD. Multicrystalline nature of drug was observed in pure drug sample whereas crystalline nature was observed in optimized formulation. Drug release was observed to follow Korsmeyer peppas model of kinetics with R^2 value 0.996 and fickian diffusion. Surface and contour plots were also studied for dependent variables. In the accelerated stability study of one month no significant difference in disintegration time, tensile strength and drug release was found.

Keywords: Film former; Solvent casting technique; Tamsulosin hydrochloride; Xanthan gum

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INTRODUCTION

Fast dissolving wafers are a new arising oral dosage forms used by patients world widely. These dosage forms can be used even in acute condition for getting instant relief [1]. Fast dissolving wafers have gained vast attention on the market because of its various advantages along with an extended shelf life of 2-3 years [2]. These oral sublingual wafers are nothing but a thin oral strip which when place in the sublingual cavity dissolves immediately due to presence of saliva in the mouth by releasing medicament within short span of time [3]. Sublingual wafers seem to be highly advantageous dosage form during travelling as it does not need water for engulfment [4]. Even rapid onset of action is achieved as this dosage form is highly efficient in avoiding first pass metabolism. Wafers are administered sublingually to improve the onset of action, lower the dose and enhance efficacy of the medicament [5], it is more stable, durable and quicker dissolving than other conventional dosage forms, an oral wafer helps to enhance bioavailability of the drug [6], improves dosing accuracy i.e., single unit dosage form [7], has the potential to allow the use of bitter tasting drug into the formulation and improves patient compliance [8,9]. Benign prostatic hyperplasia is a condition in which there is enlargement of prostate gland without malignancy. The bladder wall thickens and loses the ability to empty completely. Tamsulosin hydrochloride causes relaxation of smooth muscles of prostate and bladder neck to improve urine flow and to reduce bladder outlet obstruction. This disorder is seen mainly at the age of 40-45 years in the patient.

MATERIALS AND METHODS

Materials

Tamsulosin hydrochloride was obtained as a gift sample from Wockhart Pvt Ltd, Aurangabad, India. Xanthan gum was purchased from Balaji Drugs, Gujarat, India. Fast dissolving oral sublingual wafers were prepared by using film former with polyethylene glycol 400 as plasticizer. All other chemicals were of analytical grade.

Methods

Characterization of drug and excipient:

Fourier-transform infrared spectroscopy (FT-IR): Drug sample was characterized by FTIR spectroscopy. The spectrum was recorded using potassium bromide (KBr) with Tamsulosin hydrochloride-KBr mixture triturated in ratio 1:300 respectively by using FTIR spectrophotometer (Jasco MV 4100). The scanning range was 4000 to 600 cm^{-1}. The spectrum was compared with the reported functional group of drug structure [10]. The same was done for xanthan gum.

Differential scanning colorimetry (DSC): The DSC thermogram of Tamsulosin hydrochloride was recorded using differential scanning colorimeter (DSC 1, Mettler Toledo, Japan). Approximately 2-5 mg of sample was heated in a pierced aluminium pan (Al-Crucible, 40 Al) from 30-300°C at a heating rate of 10°C/min under a stream of nitrogen at flow rate of 50 ml/min. Thermal data analysis of the DSC thermogram was conducted using STAR^e Software (version 5.21).

Preparation of sublingual wafers by solvent casting technique: A 14 ml solution of xanthan gum, polyethylene glycol 400 (PEG 400), cross carmellose sodium as super disintegrant, ethanol and sodium saccharine was made by solvent casting technique with ice cold distilled water and sublingual wafers were prepared. Drug solution was sonicated for 30-45 min to solubilize the drug completely in the solvent. Drug solution was poured into polymeric solution and ethanol was added for alkaline hydrolysis. Both solutions are uniformly mixed to get a homogeneous solution on magnetic stirrer at 250-320 rpm. Then this solution was spread on film former by adjusting the desired temperature. Once the wafer sheet was ready, it was cut into desired size of 1.5 cm × 2 cm was dried and was removed with help of spatula and dried in oven if required. The composition of sublingual wafers is given in Table 1.

Table 1: Composition of fast dissolving sublingual wafers of tamsulosin hydrochloride

Sr. No	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Drug (mg)	26	26	26	26	26	26	26	26	26
2	Xanthan gum (mg)	70	50	70	70	50	50	90	90	90
3	PEG 400 (ml)	0.5	0.8	0.8	1	0.5	1	1	0.8	0.5
4	Ethanol (ml)	1	1	1	1	1	1	1	1	1
5	Cross carmellose sodium (mg)	200	200	200	200	200	200	200	200	200
6	Sodium Saccharine (mg)	45	45	45	45	45	45	45	45	45
7	Distilled water(ml) (Temp-14-16°C)	14	14	14	14	14	14	14	14	14

Evaluation Parameters for Oral Sublingual Wafers

Mechanical properties:

Mechanical properties of the films were evaluated using tinius olsen tensile tester (model-T-138B).

Tensile strength:

It is the maximum stress applied to a point at which the sublingual wafer specimen breaks. It is calculated by the applied load at rupture and then divided by the cross-sectional area of the strip as given in the equation below: [11]

Tensile strength = Load at Failure × 100/ (wafer thickness × wafer Width)

Percent elongation:

When the stress is applied, a wafer sample stretches and this is referred to as strain. Strain is basically the deformation of wafer divided by original dimension of the sample. Generally elongation of strip increases as the plasticizer content increases [12].

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

Thickness of the film:

The thickness of wafer was calculated by using vernier calliper. Vernier calliper was set to zero the insert the sublingual wafer and tighten the screws For this a 1.5 cm × 2 cm sublingual wafer was cut and average reading for 20 such wafers were calculated [13].

Weight variation of the film:
To determine weight of each sublingual wafer of an area of 1.5 cm × 2 cm was cut from different locations of sublingual wafer and was weighed on electronic pan balance. Average of 20 wafers was calculated.

Folding endurance:
The folding endurance was determined by repeatedly folding one sublingual wafer at the same place till it broke. The number of times the wafer could be folded at the same place without breaking gives the value of the folding endurance [14].

pH of wafer:
The wafer to be tested was placed in a Petri dish and was moistened with 0.5 ml of distilled water. The pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and kept for 1 min to allow equilibrium condition and the reading on the pH meter was noted [15,16].

***In vitro* disintegration time:**
Disintegration time is the time when a wafer breaks or starts to disintegrate. A wafer of 1.5 cm × 2 cm was cut and was put in the beaker containing 50 ml distilled water. The time when sublingual wafer was completely disintegrated noted as disintegration time. The standard value for disintegration time is within 1 min for fast mouth dissolving wafer [17,18].

Drug content:
A wafer of 1.5 cm × 2 cm was cut and put into 100 ml phosphate buffer of pH 6.8 and was continuously stirred at rpm 400-500 for about an hour. After an hour stirring was stopped and content was transferred to 10 ml volumetric flask and absorbance was measured in UV-Visible spectrophotometer [19]. The absorbance was noted above 1 µg/ml it was further diluted with phosphate buffer pH 6.8 at 224 nm and reading was noted.

***In-vitro* drug release:**
In vitro dissolution study was done using phosphate buffer pH 6.8 of 900 ml using paddle apparatus II. Film of size 1.5 cm × 2 cm was cut and put into the dissolution chamber and rotations per minute was set to 50 and temperature of 37 ± 2ºC. Sampling was done for 5 minutes at interval of 0, 10, 15, 20, 25, 30, 45 seconds. The solution so withdrawn was filtered. Absorbance was measured on UV spectrophotometer at 224 nm [20-22].

Differential scanning colorimetry (DSC):
The DSC thermogram of optimized formulation was recorded using Differential scanning colorimeter (DSC 1, Mettler Toledo, Japan). Approximately 2-5 mg of sample (i.e., optimized formulation) was heated in a pierced aluminium pan (Al-Crucible, 40 Al) from 30-300°C at a heating rate of 10°C/min under a stream of nitrogen at flow rate of 50 ml/min. Thermal data analysis of the DSC thermogram were conducted using STAR^e Software (version 5.21).

Powder X-ray diffraction analysis (XRD):
For XRD drug sample and optimized formulation was studied using X-ray diffractometer. The optimized formulation was subjected to powder XRD. To study X-Ray diffraction pattern, the sample was placed into aluminium holder and the instrument was operated between initial and final 2θ angle of 3-80° respectively in an increment of 2θ.

RESULTS AND DISCUSSION

Characterization of Drug and Excipients
Fourier transform infrared spectroscopy:
IR spectra of tamsulosin hydrochloride and its physical mixtures with formulation excipients were determined using FTIR and are presented in Figures 1-3 respectively.

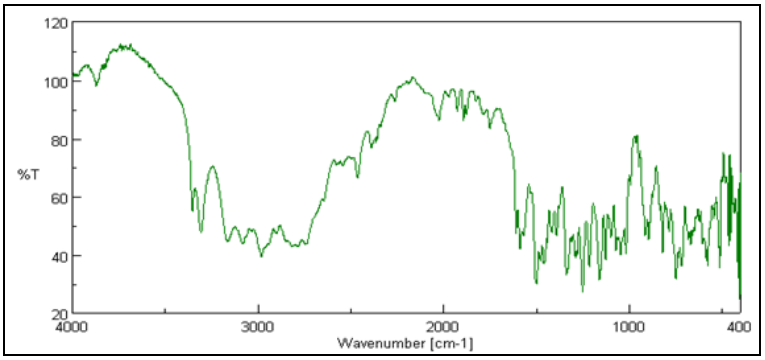

Figure 1: FT-IR of tamsulosin hydrochloride

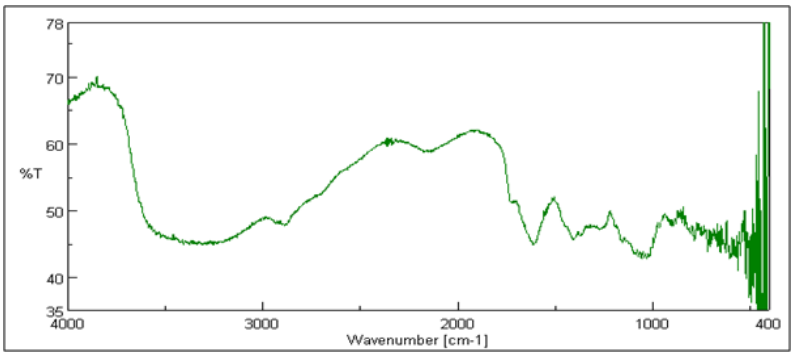

Figure 2: FT-IR of xanthan gum

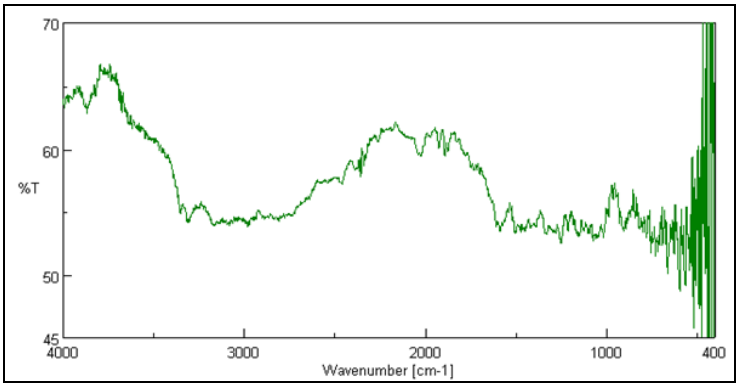

Figure 3: FT-IR of physical mixture

Pure tamsulosin hydrochloride spectrum showed sharp characteristic peaks at 2981 cm^{-1} (-C-H stretching), at 2025 cm^{-1} (C=C), 3307 cm^{-1} (S-N) and 1337 cm^{-1} (-SO_2 group). FTIR spectra of tamsulosin hydrochloride and its physical mixture (Figure 3) with excipients showed the same characteristic bands of the drug in the same regions and at the same ranges, indicating that there was no interaction between the drug and excipients used [23]. DSC thermo gram of Tamsulosin hydrochloride as shown in Figure 4 indicates sharp endothermic peak Tp (temperature of peak) at 233ºC (Actual melting point 228ºC) corresponds to the melting point of Tamsulosin hydrochloride [24,25].

Evaluation of Sublingual Wafers

Mechanical properties:

Tensile strength: From the results it was clear that when the concentration of xanthan gum increases, the tensile strength of the sublingual wafer also increases. The tensile strength of the wafer was found to be in the range of 12.58 ± 0.063 (formulation F1) to 27.33 ± 0.325 (formulation F8) as shown in Figure 5. The formulation F8 showed tensile strength 27.33 ± 0.325 which made it the best formulation among the all. This result may be due to the presence of polymer in more concentration. The tensile strength of wafers made with natural polymer is high but here its low because of using a natural polymer for forming sublingual wafer.

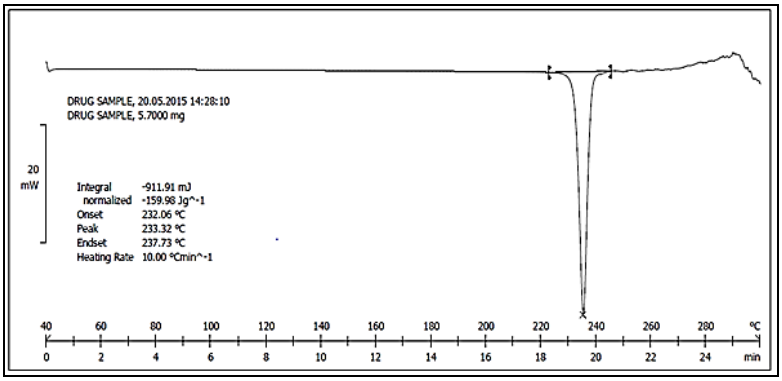

Figure 4: DSC of tamsulosin hydrochloride

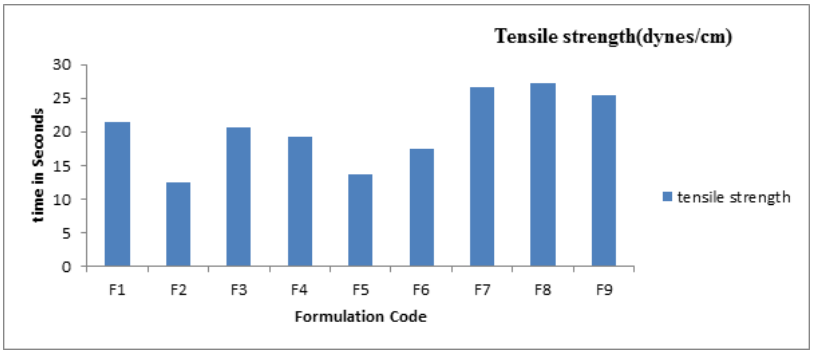

Figure 5: Average tensile strength of different formulations (F1-F9)

Percent elongation: The wafer of area 2 cm × 1.5 cm was taken for carrying out percent elongation. It was seen that as concentration of plasticizer PEG 400 increases the value of percent elongation aslo increases. Formulation F8 has 19.80 ± 0.304 value of percent elongation whereas formulation F5 has lowest value which is 7.57 ± 0.678. Percent elongation of all formulations is shown in Figure 6.

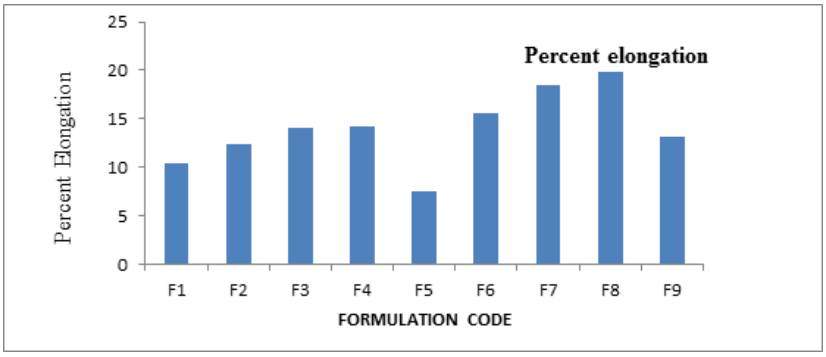

Figure 6: Average percent elongation of different formulation (F1-F9)

Thickness: The thickness of the drug loaded sublingual wafers from F1 to F9 formulations were measured with the help of vernier caliper at different strategic locations like four corners and centre of the each wafers. Mean SD was calculated. Thickness should be controlled within a ± 5% variation of standard value. The thickness of wafer varies from formulation F1 0.08 ± 0.0130 mm to formulation F9 0.128 ± 0.027 mm as statesd in Table 2. Formulation F8 was having the thickness of 0.146 ± 0.013 mm which was good. From above data it was concluded that thickness of wafer increases as concentration of xanthan gum increases.

Weight variation of the wafer: The weight of each film of 2 cm × 1.5 cm was taken on electronic weighing balance. Mean S.D was also calculated. From the Table 2 given below it was concluded that the weight of the wafer increases as the concentration of polymer increases. The weight variation ranges from 16.314 ± 0.163 for the F1 formulation to 20.44 ± 0.216 for F9 formulation. The Indian pharmacopoeial limit for weight variation is ± 10%. Formulation F8 was having weight of 22.40 ± 0.2959 which was highest. Overall, the weight of wafer made with nautral polymer was seen to be less when compared with film made by using natural polymers.

Folding endurance: The wafer of size 1.5 cm × 2 cm was repeatedly folded at the same place until it breaks and the number of time the sublingual wafer could be folded without breaking was noted as folding endurance of the wafer. The value of folding endurance from 189±0.816 for formulation F1 to 212±0.547 for formulation F9 as mentioned in Table 2.

Table 2: Apperance, weight veriation, thickness and folding endurance of factorial batches (mean ± S.D)

Formulation Code	Appearance(n=3)	Thickness (n=5) (mm)	Weight Variation (n=5)	Folding endurance (n=5)
F1	Semitransparent, smooth, thin	0.08 ± 0.0130	16.314 ± 0.163	189 ± 0.816
F2	Thin, smooth, semitransparent	0.078 ± 0.016	13.184 ± 0.129	158 ± 0.836
F3	Semitransparent, thin, smooth	0.076 ± 0.020	15.546 ± 0.101	183 ± 1.303
F4	Smooth, thin,Semintransparent	0.113 ± 0.0130	14.360 ± 0.108	190 ± 0.894
F5	Thin, smooth, semitransparent	0.027 ± 0.083	13.394 ± 0.101	165 ± 0.707
F6	Smooth, thin, Semintransparent	0.06 ± 0.0158	12.584 ± 0.149	168 ± 0.836
F7	Semitransparent, thin, smooth	0.116 ± 0.013	18.344 ± 0.080	198 ± 1.30
F8	Smooth, thin, Semintransparent	0.146 ± 0.013	22.402 ± 0.2959	210 ± 0.547
F9	Thin, smooth, Semitransparent	0.128 ± 0.027	20.448 ± 0.216	212 ± 0.547

pH of the wafer: As shown in Table 3 pH value lies betweenformulation F1 6.8 ± 0.01 to formulation F9 6.8 ± 0.0264. The pH value for formulation F8 batch is 6.9 ± 0.0251 which was in the pH range of saliva 6.5 to 7.5 which is suitable for sublingual wafer to dissolve and release medicament.

***In vitro* disintegration time:** Disintegration time was calculated by dropping the wafer in 25 ml beaker containing distilled water and time when the wafer was completely disintegrated was noted. The faster is disintegration of wafer faster will be the release which may help to achive faster onset of action. The disintegration time for formulation F1 was 8 ± 0.577 seconds to formulation F9 17 ± 0.573 seconds as performed and presented in Figure 7. The F8 batch has disintegration time of 20 ± 0.577 sec which is feasible. These values are mentioned in Table 3. From all results below it can be conlcluded that as the polymer concentration increases the disintegration time of the sublingual wafer also increases. The decrease in disintegration time was due to swelling of polymer as ice cold solution distilled water was used while preparing homogeneous solution for peparing sublingual wafers.

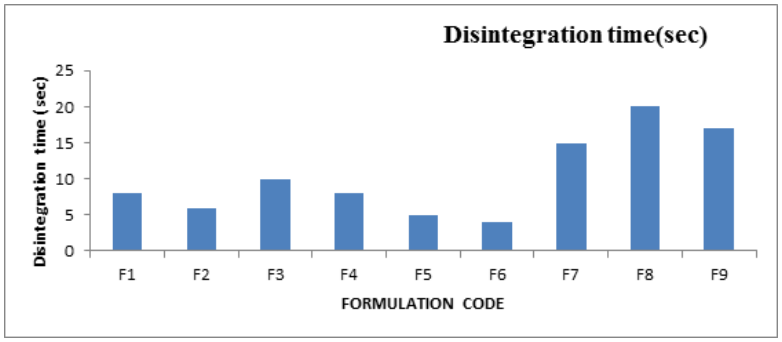

Figure 7: Average disintegration time(sec) of formulations (F1-F9)

Drug content: Drug content of factorial batches was calculated by using wafer containing 26 mg of Tamsulosin hydrochloride. Three trials from each formulation were analyzed spectrophotometrically. The mean value and standard deviation of all the formulations were calculated. Drug content of all batches, F1 to F9, was found in the range of 97.7 ± 1.275% - 99.25 ± 0.424%. The limit for specification is within the range 98.5%-101.5%. Formulation F1 and F5 are not within the limit. But Formulation F1 has drug content of 97.7 ± 1.275 and formulation F5 has 97.08 ± 0.735 as shown in Table 3. It shows that higest amount of drug is incorporated in F8 formulation. Hence, only formulation F1 and F5 do not comply with the standard drug content and rest all formulations are in the range [10,24].

Table 3: pH, disinteragation time and drug content of factorial batches(mean ± S.D)

Formulation Code	pH (n=3)	Disintegration Time (sec) (n=3)	Drug Content (%) (n=3)
F1	6.8 ± 0.01	8 ± 0.577	97.7 ± 1.275
F2	6.4 ± 0.015	6 ± 0.577	98.5 ± 0.206
F3	6.7 ± 0.021	10± 0.707	98.56 ± 0.424
F4	6.8 ± 0.0208	8 ± 1.00	98.56 ± 1.123
F5	6.5 ± 0.0360	5 ± 1.527	97.08 ± 0.735
F6	6.4 ± 0.0378	4 ± 0.5773	98.75 ± 1.123
F7	6.8 ± 0.0404	15 ± 1.00	98.79 ± 1.530
F8	6.9 ± 0.0251	20 ± 0.577	99.25 ± 0.424

F9	6.8 ± 0.0264	17 ± 0.573	98.78 ± 0.849

***In-vitro* drug release:** *In vitro* dissolution studies were performed using phosphate buffer pH 6.8 as dissolution medium and dissolution apparatus USP Type-II (Paddle type) at 75 rpm and temperature of 37.5 ± 2ºC, to compare the release of drug from different formulations (F1-F9). By comparing all the formulations, it was concluded that formulation F8 showed the highest drug release and hence was selected as the best formulation (Figure 8). Formulation F8 showed maximum drug release of 101.88% at 20 seconds which was within the range [25,26]. *In vitro* drug release of all formulations is shown in Table 4.

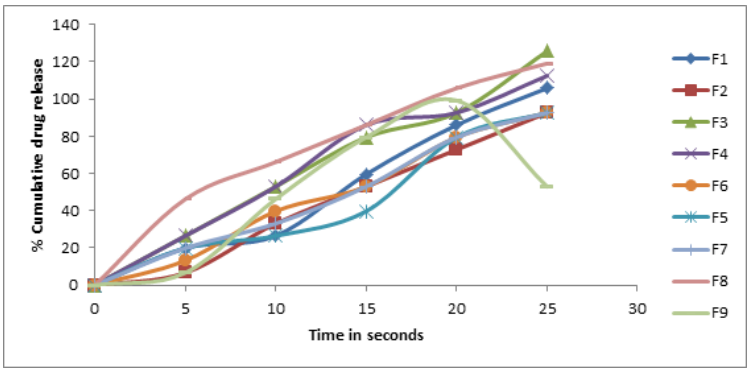

Figure 8: Graph of % cummulative drug release Vs time in seconds

Table 4: Percent cummulative drug release of factorial batches (mean ± S.D)

Formulation code	Time					
	5 seconds	10 seconds	15 seconds	20 seconds	25 seconds	30 seconds
F1	19.85 ± 0.01	26.47 ± 0.01	59.55 ± 0.02	86.02 ± 0.35	105.8 ± 0.09	79.41 ± 0.08
F2	6.61 ± 0.09	33.08 ± 0.07	52.94 ± 0.05	72.79 ± 0.01	92.64 ± 0.03	39.70 ± 0.05
F3	26.47 ± 0.02	52.94 ± 0.07	79.41 ± 0.04	92.64 ± 0.01	125.7 ± 0.08	86.02 ± 0.09
F4	26.47 ± 0.02	52.94 ± 0.07	86.02 ± 0.04	92.64 ± 0.06	112.5 ± 0.09	46.32 ± 0.02
F5	19.85 ± 0.06	26.47 ± 0.09	39.70 ± 0.03	79.41 ± 0.06	92.64 ± 0.02	112.5 ±0.02
F6	13.23 ± 0.02	39.70 ± 0.03	52.94 ± 0.01	79.41 ± 0.01	92.64 ± 0.08	99.26 ± 0.02
F7	19.85 ± 0.09	33.08 ±0.06	52.94 ± 0.08	79.41 ± 0.07	92.6 ± 0.04	105.8 ± 0.05
F8	46.23 ± 0.01	66.17 ± 0.08	86.02 ± 0.03	101.8 ±0.04	119.1 ± 0.03	45.66 ± 0.03
F9	6.61 ± 0.07	46.32 ± 0.08	79.45 ± 0.01	99.26 ± 0.09	52.94 ± 0.05	26.47 ± 0.06

DSC: Differential scanning colorimetric Spectra allows us to check the incompatibilities and shift in endotherm and exothermic peaks. DSC Spectra of optimized batch F8 is shown in the Figure 9 with peak at 97.84ºC. There was decrease in melting point of the final formulation these may be due to presence of other excipients in the solution of final formulation.

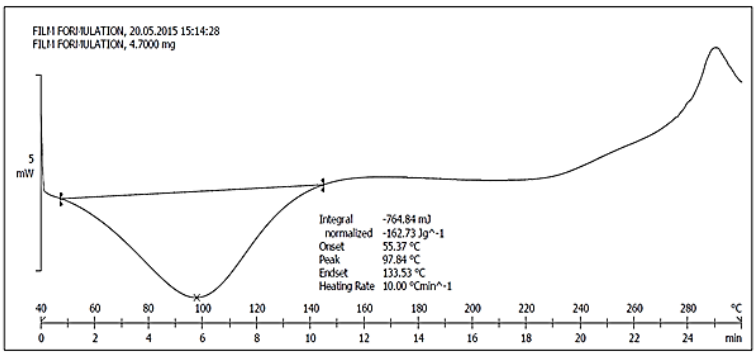

Figure 9: DSC of F8 optimized formulation

XRD: The powder X-Ray Diffraction gives the information about the crystalline nature of the substance and also the interaction between the drug and excipients. The XRD graph of Tamsulosin hydrochloride, Figure 10, showed numerous peaks which gave an indication of crystalline nature of the drug. Figure11 shows XRD graph of formulation F8. Sharp peaks of drug were observed in the final formulation.

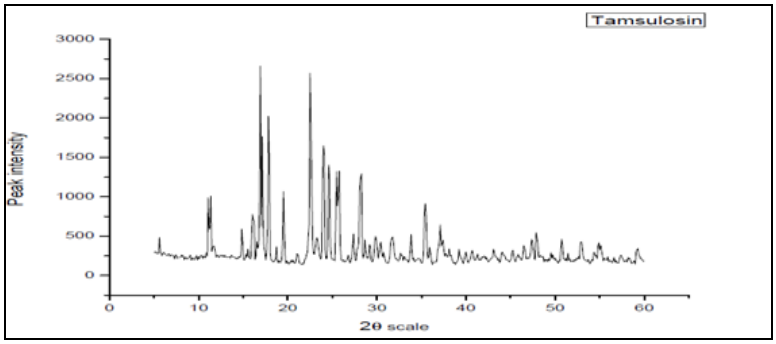

Figure 10: XRD of tamsulosin hydrochloride

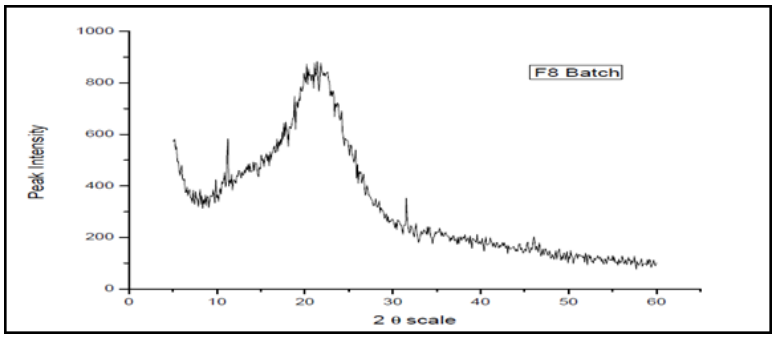

Figure 11: XRD of F8 optimized batch

Generation of Statistical Models

A statistical model, $Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X^2 + b_{11}X_1^2 + b_{22}X_2^2$ incorporating interactive and polynomial terms was used to evaluate the responses. The data clearly indicates that the disintegration time, % drug release and folding endurance values are strongly dependent on the selected independent variables. The fitted full equations relating the responses disintegration time, % drug release and folding endurance values to the transformed factors are as:

$$\text{Disintegration time} = -8.42544+0.308X_1-3.6842X_2$$
$$\text{\% Drug Release} = +28.88-0.12917X_1+1.3596X_2$$
$$\text{Folding endurance} = 115.144+1.0750X_1-5.87719X_2$$

Contour Plots and Response Surface Plots for Dependent Variables

If the contour plot shows the curve line it may indicate that there may be interaction in two dependant variables and if there is straight line it may indicate that there is no possible interaction between these two variables. Below Figures 12-14 shows the straight line in contour plot it may conclude that there is no interaction between these two dependant variables [24].

From the response surface plot for disintegration time in Figure 12 it is concluded that both polymer and plasticizer are directly proportional to the disintegration time. Therefore as the concentration of polymer and plasticizer increases there will be an increase in disintegration time.

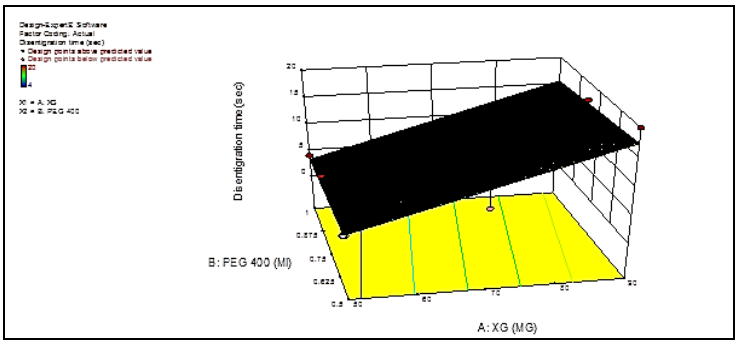

Figure 12: Response surface graph and contour plot for disintegration time

As concentration of polymer increases the drug release decreases and as plasticizer concentration increases drug release increases. Hence from Figure13 it can be concluded that polymer concentration is inversely propotional to drug release. This may be due to formation of hydrogen bonds which is seen clearly in response surface plot for drug release.

The concentration of polymer is mainly responsible for increase in folding endurance as seen from the surface plot in Figure 14. Also a slight variation is shown by gradually increasing the plasticizer concentration.

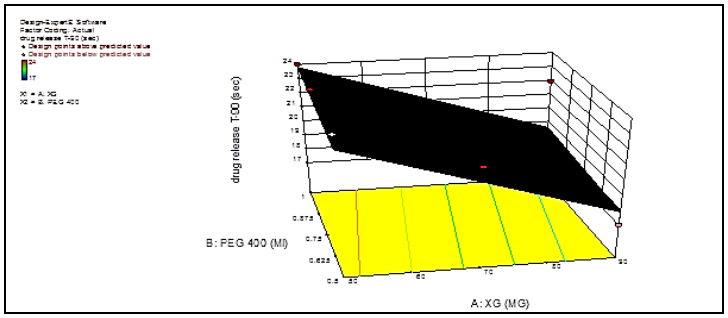

Figure13: Response surface graph and contour plot for drug release

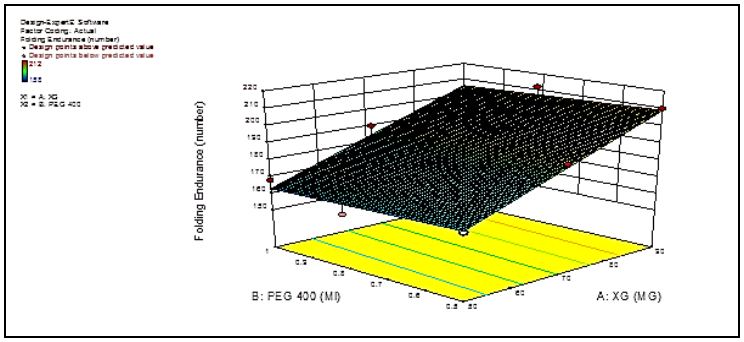

Figure14: Response surface graph and contour plot for folding endurance

Statistical Analysis of Data and Interpretation

To find out which model best fitted the formulations all the models i.e. zero order kinetics, Korsmeyer peppas model, first order kinetics and Higuchi model were applied to the formulations and value of regression coefficient was obtained. From the R^2 value the value which was almost near to 1 was selected as the best suitable model among the nine formulations. The value of release exponent (n) also helps to determine the drug release mechanism [27]. The R^2 value for all formulations (F1-F9) for zero order kinetics, korsmeyer peppas model, first order kinetics and Higuchi model was calculated. The R^2 value for korsmeyer peppas model for formulation F7 was 0.991 was found to be minimum and formulation F8 was 0.996 which was maximum. Also n value for formulation F8 following korsmeyer peppas model was calculated and it showed that it follows fickian diffusion. After applying data to the models Formulation F8 was found to be the best optimized formulation with correlation coefficient value of 0.996 and n value 1.025. Correlation of coefficient value should be almost near to 1 and if n (release exponent) <1 it follows fickian diffusion. And if n>0.5 it follows non-fickian diffusion. It is clear from above data that F8 follows Fickian diffusion and Korsmeyer peppas model is best suited for this formulation as the value of R^2 is 0.996 which is approx 1. Hence release of drug from the fast dissolving oral wafer follows fickian diffusion.

Accelerated Stability Study

Accelerated stability study was carried out for the optimized formulation. Sublingual wafers in triplicate forms were kept in the stability chambers at different conditions. Sublingual wafers were kept at following temperature 25ºC ± 60% RH, 30°C ± 65% RH and 40ºC ± 75% RH for one month to access their stability. At first the wafers were wrapped in aluminum foils and kept in stability chamber but they soften after 7 days. So in order to avoid the softening these wafers were wrapped in butter paper and kept in the stability chamber [28]. The results for accelerated stability study are shown in Tables 5 and 6.

Table 5: Accelerated stability study showing thickness, weight variation and pH (mean ±S.D) (n=3)

Time	Thickness	Weight variation	pH
Initial	0.146 ± 0.013	22.4 ± 0.295	6.9 ± 0.0251
15 Days			
25ºC ± 60%RH	0.118 ± 0.067	20.1 ± 0.015	6.8 ± 0.056
30ºC ± 65%RH	0.108 ± 0.045	19.23 ± 0.012	6.7 ± 0.089
40ºC ± 75% RH	0.102 ± 0.014	18.98 ± 0.067	6.8 ± 0.078
30 Days			
25ºC ± 60RH	0.107 ± 0.078	18.5 ± 0.089	6.7 ± 0.034
30ºC ± 65%RH	0.101 ± 0.089	17.85 ± 0.054	6.5 ± 0.025
40ºC ± 75% RH	0.98 ± 0.056	14.21 ± 0.012	6.7 ± 0.016

Table 6: Accelerated stability study showing drug release, folding endurance and disintegration (mean ±S.D) (n=3)

Time	Drug release	Folding endurance	Disintegration time
Initial	101.88	210 ± 0.547	20 ± 0.577
15 Days			
25ºC ± 60RH	98.33	190 ± 0.089	16 ± 0.081
30ºC ± 65%RH	96.89	198 ± 0.057	15 ± 0.075
40ºC ±75% RH	97.23	194 ± 0.014	11 ± 0.012
30 Days			
25ºC ± 60RH	82.34	188 ± 0.051	13 ± 0.017
30ºC ± 65%RH	80.03	189 ± 0.078	12 ± 0.056
40ºC ± 75% RH	85.49	185 ± 0.056	9 ± 0.009

CONCLUSION

Fast dissolving sublingual wafers containing Tamsulosin hydrochloride for treatment of benign prostatic hyperplasia were developed by using film former with xanthan gum as polymer. The main hurdle to make a mouth dissolving wafers by using natural gum as polymer was tackled by adjusting the temperature of solvent to 14-16°C i.e. distilled water which helped the polymer to swell thereby the quantity of polymer required for forming sublingual wafer. It was possible to prepare sublingual wafer successfully by 3^2 factorial design. Therefore, the formulation F8 was found potential to develop sublingual wafers.

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