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Original Article

Design and Statistical Optimization of Fast-Dissolving Buccal Films of Doxylamine Succinate for Allergy Treatment

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ABSTRACT

Aim and Objectives: The present work aimed to prepare a FDBF with a fixed dose of Doxylamine succinate. This film provides fast relief from sudden allergic reactions. **Materials and Methods:** FDBF were produced employing a technique known as solvent casting. Eight different formulations were tested in an experiment where we varied three factors: X1-PVA concentration, X2-PVP concentration and X3-PG concentration. The two responses were: Y1-disintegration time (sec) and Y2-cumulative drug release (%). Each formulation was subjected to a range of evaluations, including weight variation, folding endurance, thickness, drug content and *in vitro* studies. Statistical analysis of the responses was performed using Design Expert software version 13.0 trial edition. **Results:** All the formulations of the films were transparent, non-sticky and could be easily peeled off. They satisfactory exhibited all the evaluation parameters. The concentration of the PVA, PVP and PG was observed to significantly influence on both the disintegration time and drug release. The optimized formulation OF1, dissolved in 68 sec and drug released at 71.5%. *Ex vivo* testing on goat buccal mucosa showed a drug release rate of 73.3%. The results of the short-term stability test of optimized formulation OF1 according to the International Council for Harmonization guidelines confirmed that the product stays stable for one month at temperature of 30ºC±2ºC and relative humidity of 65%±5%. **Conclusion:** Based on these results, it can be concluded that FDBF present a promising drug delivery approach for DOXS bypassing first-pass metabolism. This facilitates rapid drug permeation, improving absorption and bioavailability.

Keywords: Doxylamine succinate, Fast dissolving buccal films, PVA, Statistical analysis.

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INTRODUCTION

Doxylamine succinate is chemically identified as N, N-dimethyl-2-(1-phenyl-1-pyridin-2-yl-ethoxy)-ethanamine, is primarily utilized as an antihistamine medication. It is marketed as a succinate salt and is classified as a first-generation H1 receptor antagonist within the ethanolamine group.[1] DOXS is known for its strong sedative effects and is used to treat allergies, nausea and insomnia. It has also been used in veterinary medicine and also used to treat Parkinson's disease. It's frequently combined with painkillers, cough medicines and antihistamines to alleviate symptoms like body aches, coughing, fever, headaches, runny nose and sneezing associated with colds. Half-life is 2-3 hr and an absolute oral bioavailability of approximately 24.7%. The study was focused on improving the bioavailability and therapeutic impact of DOXS by formulating FDBF.[2]

FDBF are comprised of thin rectangular or square-shaped strips, typically positioned on the patient's buccal layer or any oral mucosal tissue, where they quickly moisten upon contact with saliva. Subsequently, the film rapidly hydrates, releasing the Active Pharmaceutical Ingredient (API) within minutes. This mechanism allows for rapid absorption and immediate bioavailability of drugs, facilitated by the abundant blood flow and permeability of the oral mucosa. Buccal films serve as a valuable option for various patient groups, including paediatric, geriatric, bedridden, emetic, diarrheal and individuals experiencing sudden allergic attacks.[3]

Oral Fast Dissolving Film (OFDF) offers a new way to improve consumer acceptance with its quick dissolution and ease of self-administration without the need for water or chewing. It serves as a quick-dissolving drug delivery system in the mouth, meeting market needs with its easy handling, uncomplicated packaging and reduction of unpleasant tastes. The film, placed on the tongue, remains in position and promptly releases the active ingredient for absorption. Developing fast-dissolving films also opens opportunities for expanding product lines, as a wide range of drugs can be considered for this dosage form, includes

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various types of medications such as analgesics, neuroleptics, anti-asthmatics cardiovascular drugs, antihistamines and treatments for erectile dysfunction.[4] In this study, mucoadhesive buccal films containing DOXS were designed and developed to treat allergies. The formulation involved integrating the drug into a compatible polymer system, aiming to enhance patient convenience and compliance.[5]

MATERIALS AND METHODS

Materials

Doxylamine succinate was purchased from Yarrow Chem Products, Mumbai, Maharashtra, India. PVA, PVP, PG, Polysorbate 80, Mannitol, Citric acid was obtained from Department of Pharmaceutics, Hubballi. All chemicals utilized in this study were of analytical grade.

Methods

Determination of dose of drug

$$Dose\ of\ drug = \frac{oral\ dose\ \times oral\ bioavability}{body\ surface\ area}$$

Area of rectangular mould is A=lxb

$$A=7.8x5.2=40.56\ cm^2$$

Area of square film is 1.5x1.5=2.25 cm^2.

$$\text{Total number of films in each mould } \frac{40.56}{2.25} = 18.22\,cm2$$

A single film holds 10 mg of the drug, while 18.22 films contain 182.2 mg of the drug.

Dose per mould=Dose per film×Area of mould/size of 1 film.

So, one mould containing 182.2 mg drug.

Experimental design

An experimental layout was established with eight formulations, three factors, each having two levels. The independent variables selected for the study were the concentrations of PVA (X1), PVP (X2) and PG (X3). The dependent variables chosen were disintegration time (Y1) measured in seconds and cumulative drug release (Y2) measured in percentage.[6] Table 1 outlining the arrangement of the experimental design.

Formulation of FDBF

FDBF were produced utilizing the solvent casting methodology. Measured amounts of PVA polymers were added to a beaker containing an appropriate quantity of the organic phase. The solution was stirred for 2 hr, during which weighed quantities of the drug (DOXS) and Plasticizer (PVP) were added to the polymeric solution with continuous stirring. Additional excipients such as citric acid, PG, Polysorbate 80 and mannitol were added and thoroughly mixed, ensuring the absence of air bubbles. The resulting homogeneous mixture was then casted onto a clean and dry rectangular mould previously lubricated with glycerine. The volume of solution required for pouring into the mould was carefully determined. After casting, the filled rectangular mould was for 24 hr drying period in a hot air oven maintained at 60°C. Following drying, the film was carefully removed from the mould and cut into pieces measuring 1.5×1.5 cm^2 each. Films with any imperfections were excluded from further evaluation. The final samples of films were individually wrapped in butter paper followed by aluminium foil and stored appropriately until needed.[7,8] The formulation is detailed in Table 2.

RESULTS

Preformulation

Determination of wavelength of maximum absorption (λ_{max})

A solution containing DOXS at a concentration of 10 µg/mL was prepared by dissolving it in a buffer solution with a pH of 6.8. UV spectrum analysis was performed using a Shimadzu (UV-1900i) double beam spectrophotometer, scanning the solution within the wavelength range of 200-400 nm. The absorption maximum was found to be 261 nm using 6.8 pH buffer solution observed in Figure 1.[6]

Preparation of standard calibration curve

25 mg of DOXS was dissolved in 25 mL of pH 6.8 buffer to create a stock solution-I at 1 mg/mL. From this, 2.5 mL was withdrawn then diluted to 25 mL to make stock solution-II at 10 µg/mL. Aliquots of 1.0 to 6.0 mL were withdrawn from stock solution-II and diluted to 10 mL to obtain concentrations of 10 to 60 µg/mL. The absorbance values for these solutions were determined at a wavelength of 261 nm using a UV spectrophotometer, as detailed in Table 3. Finally, a graph of concentration in µg/mL v/s absorbance in nm was plotted shown in Figure 2.[1]

Differential Scanning Calorimetry

DSC measurements were done using a DSC 60 plus, Shimadzu, Japan to analyze the thermal properties of the pure drug. Samples of precisely 5 mg were sealed in standard aluminum pans and subjected to heating under a flow of nitrogen gas (20 mL/min). The temperature ramped at 10°C/min from 0 to 150°C. The observed melting point of 106.78°C falls within the standard range of 100°C to 108°C was shown in Figure 3.[6]

Determination of drug-polymer compatibility

By Fourier Transform Infrared Spectroscopy (FTIR)

A blend comprising the Active Pharmaceutical Ingredient DOXS and PVA excipients in a ratio of 1:1 was stored in bottles (amber-colored). These bottles were placed in a stability chamber set to a temperature of 30°C±2°C and a Relative Humidity (RH) of 65%±5% for a duration of one month. Following this timeframe,

Table 1: Factorial 2^3 design variables and responses with their levels.

Independent variables		
Levels used	**Lower**	**Upper**
X1=PVA	350	850
X2=PVP	150	450
X3=PG	0.2	0.8
Dependent variables		
Y1=Disintegration time		
Y2=Cumulative drug release		

Table 2: Layout of Doxylamine succinate FDBF by using DOE Software.

Sl. No.	Ingredients (mg)	Formulation Code							
		F1	F2	F3	F4	F5	F6	F7	F8
1	DOXS	182	182	182	182	182	182	182	182
2	PVA	850	350	850	350	350	850	850	350
3	PVP	150	450	450	150	150	150	450	450
4	Citric acid	500	500	500	500	500	500	500	500
5	Mannitol	30	30	30	30	30	30	30	30
6	Polysorbate 80	0.3 mL	0.3 mL	0.3 mL	0.3 mL	0.3 mL	0.3 mL	0.3 mL	0.3 mL
7	Propylene Glycol	0.8 mL	0.8 mL	0.2 mL	0.8 mL	0.2 mL	0.2 mL	0.8 mL	0.2 mL
8	Distilled water	15 mL	15 mL	15 mL	15 mL	15 mL	15 mL	15 mL	15 mL

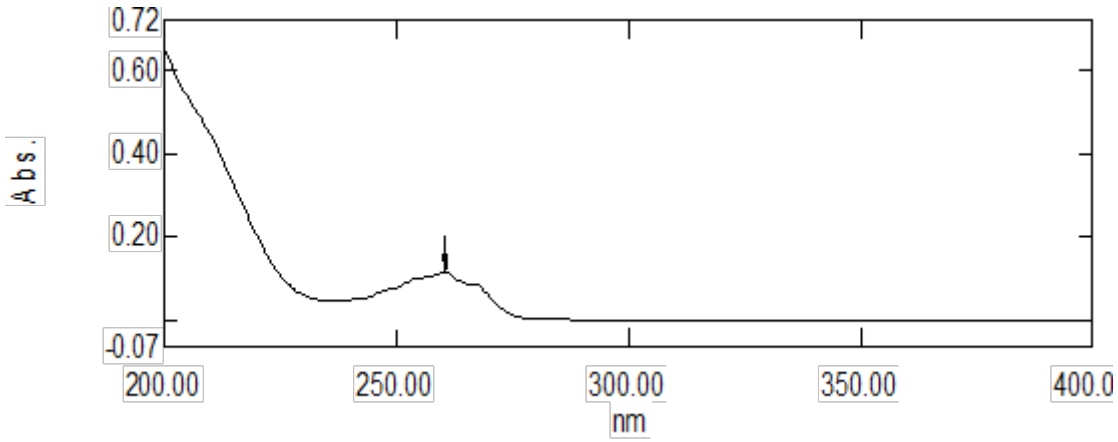

Figure 1: UV Spectra of DOXS in 6.8 pH buffer solution.

the samples analyzed using FTIR spectroscopy (FTIR-8400S, Shimadzu, Japan) within a scanning range of 3600-800 cm^{-1}. This study aimed to assess the compatibility between the API, polymer, mixture of API and polymer and optimized formulation. The FTIR spectra were shown in Figures 4-7 and the functional groups of FTIR peaks were observed in Table 4.[9-12]

Evaluations

Weight variation

Three films measuring 1.5×1.5 cm^2 were randomly selected from each film formulation. Each film was weighed individually using an electronic balance and subsequently, the average weight for each batch was calculated. The films were observed to fall within the range of 57.66±1.5 mg to 141.3±1.5 mg which was acceptable seen in the given Table 5.[13]

Folding endurance

This test is crucial for assessing the film's ability to endure folding and also serves as an indicator of its brittleness. The folding endurance of the strips was evaluated by repetitively folding a single film up to 200 times at a consistent location until it reached its breaking point. The value of folding endurance for the

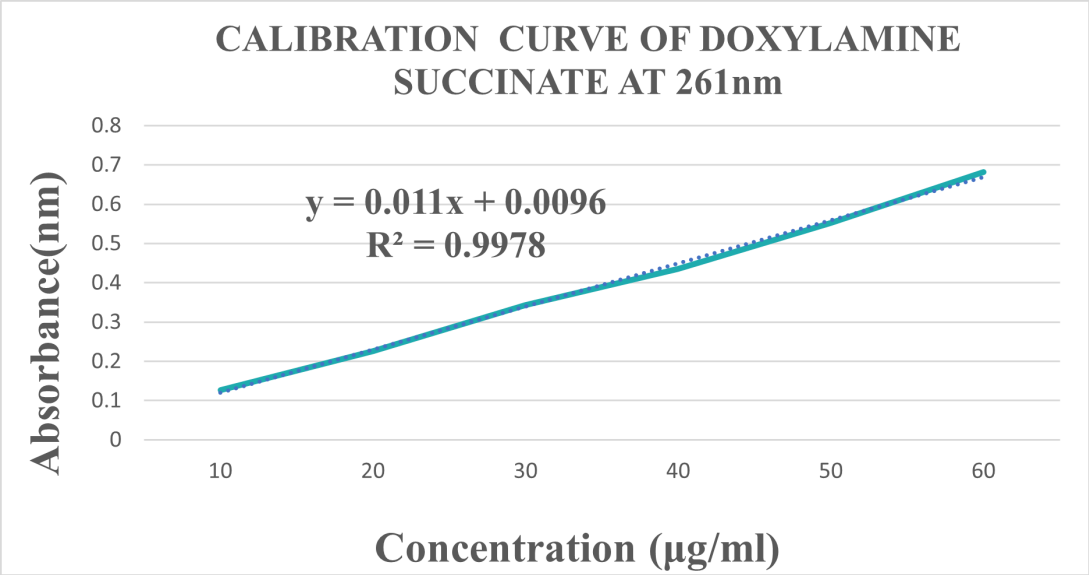

Figure 2: Calibration curve of Doxylamine Succinate.

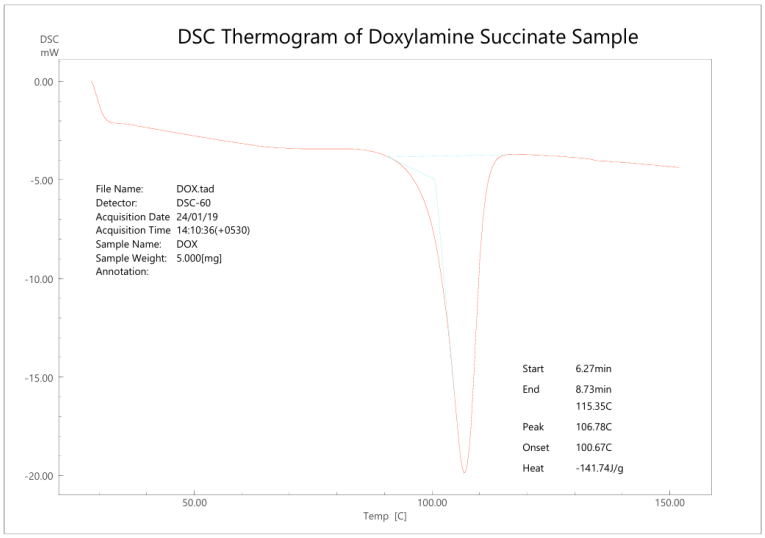

Figure 3: Thermal analysis graph of the pure drug DOXS obtained from DSC.

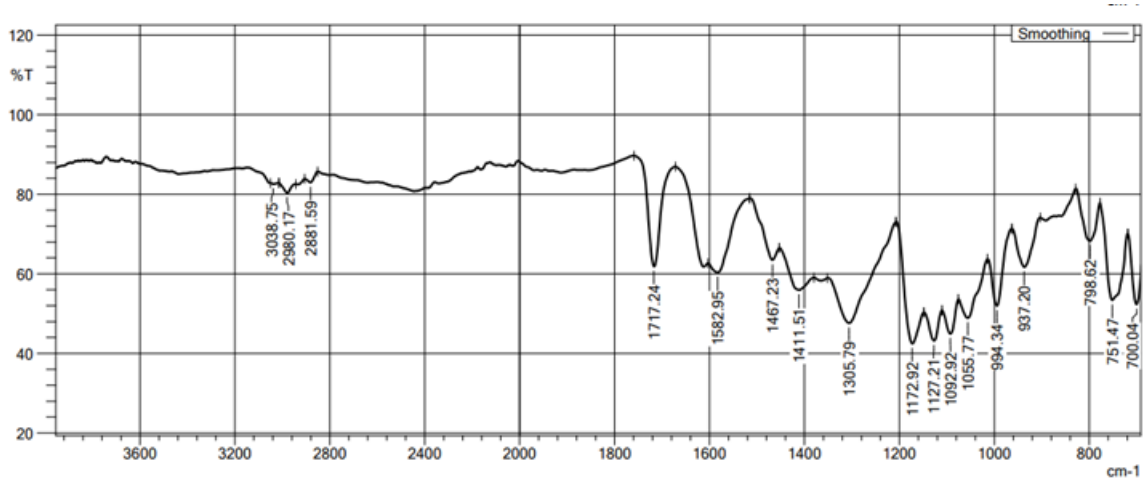

Figure 4: The infrared absorption spectrum of the pure drug DOXS.

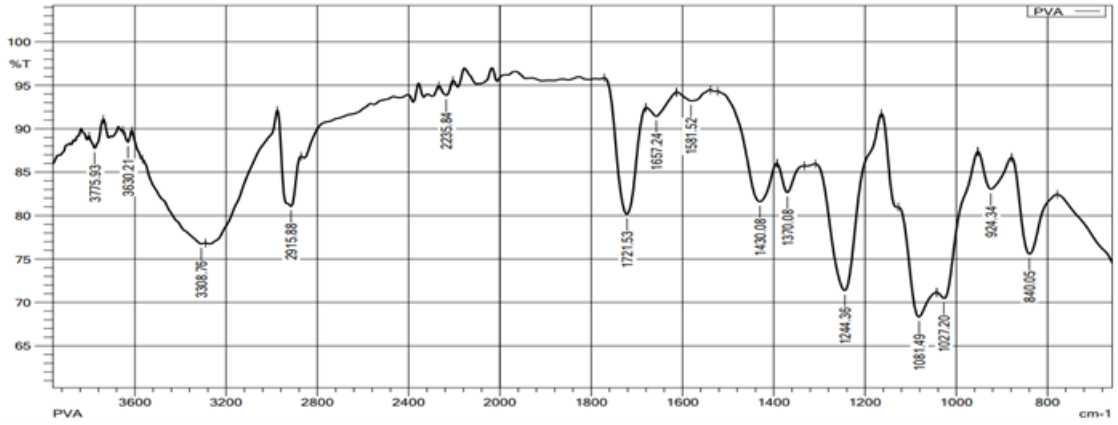

Figure 5: The infrared absorption spectrum of PVA polymer.

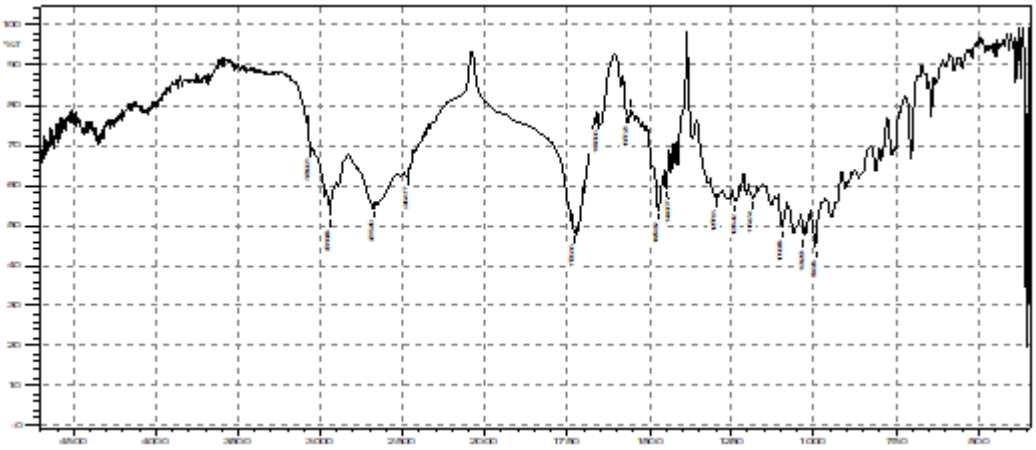

Figure 6: FTIR spectrum of mixture of DOXS and PVA.

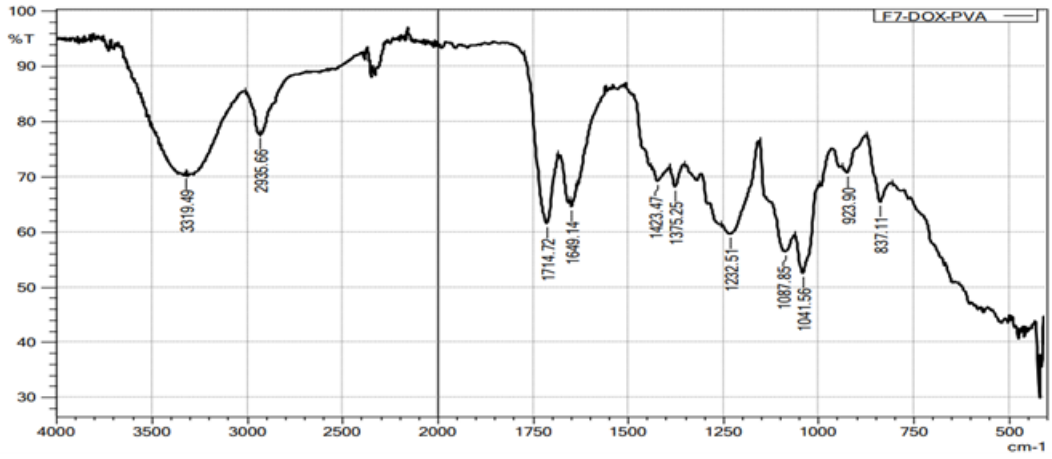

Figure 7: FTIR spectrum of Optimized formulation OF1.

prepared buccal films were found within 108±2.60 to 201±2.516 as shown in Table 5.[14]

Surface pH measurement

Since acidic or alkaline pH levels may lead to irritation of the oral mucosa, it's crucial for the film to maintain a surface pH close to neutral. It was placed in a petri dish and allowed to swell at room temperature.[15] To determine the pH, a film was dissolved in 1-2 mL of distilled water and the pH of the resultant solution was determined using pH paper, revealing a pH within the range of 6-7 as shown in the Table 5.[16]

Thickness

The film exhibited thickness ranging from 0.143±0.03 mm to 0.266±0.04 mm by micrometer screw gauge at three different places and the average of these three measurements was calculated.

This step is essential to ensure uniformity in the film thickness, as it directly impacts the accuracy of the dosage administered by the film. The results are shown in the Table 5.[17]

Drug content uniformity

To evaluate drug content uniformity, a patch with an area of 1.5×1.5 cm^2 containing API was dissolved in 100 mL of pH 6.8 solution with occasional shaking. Filtration was then performed to eliminate any insoluble residue. 5 mL of the filtrate was subsequently diluted to 10 mL with pH 6.8 solution and the absorbance was assessed at a wavelength of 261 nm using a UV Spectrophotometer. This procedure was carried out for all formulations the range of drug content by using PVA polymer ranges between 86.48% to 101.81% which was acceptable as shown in the Table 5.[14] The acceptable limit for content uniformity is between 92% and 108%. The drug content was calculated using the following formula,

$$Drug\ content = \frac{Theoretical\ yield}{Pratical\ yield} \times 100$$

Percentage moisture loss

The film under test was placed in desiccators containing activated silica. After three days, the film was removed and weighed again. This process was repeated three times to verify the results. The results of the % moisture loss were depicted in the Table 5. The percentage moisture content was determined using the following formula:

$$Moisture\ content\ \% = \frac{Wo - Wt}{Wo} \times 100$$

Table 3: Absorbance of Doxylamine succinate at 261 nm.

Concentration (µg/mL)	Absorbance at 261 nm*
10	0.127±0.0008
20	0.226±0.0004
30	0.343±0.0008
40	0.436±0.0006
50	0.553±0.0008
60	0.682±0.0002

*Mean± SD *n*=3.

Where, Wo=Initial weight and Wt=Final weight.[18]

Disintegration test

The disintegration evaluation of FDBF can be conducted using a disintegration test apparatus according to specifications outlined in the Indian Pharmacopoeia (I.P.). The disintegration evaluation of FDBF can be conducted using a disintegration test apparatus according to specifications outlined in the Indian Pharmacopoeia (I.P.). This procedure involves placing a film in each of the six tubes of the basket, adding a disc to each tube and running the apparatus with pH 6.8 (simulated saliva fluid) maintained at 37°±2°C as the immersion medium. The assembly is then moved up and down at a rate of 30 cycles/min and the time taken in seconds for complete disintegration of the film, leaving no residue in the apparatus, is observed and recorded. The disintegration times are provided in Table 6. F5 exhibited the shortest disintegration time of 16±1.0 sec, while F7 displayed the longest disintegration time of 128±0.08 sec.[19]

In vitro diffusion study

The diffusion study employed a Franz diffusion cell equipped with a dialysis membrane serving as an artificial barrier. Prior to mounting, the dialysis membrane was soaked in pH 6.8 buffer for 24 hr. A 1.5 × 1.5 cm^2 film was carefully positioned on the membrane between the donor and receptor chambers. The receptor chamber, containing 13 mL of pH 6.8 phosphate buffers as the dissolution medium, was kept in contact with the donor chamber. The setup was maintained at a temperature of 37±0.5°C. Stirring of the solution in the receptor compartment was achieved using a magnetic bead. At specified intervals, 0.6 mL (sample) was withdrawn and replaced with fresh pH 6.8 buffer solutions. These samples were subsequently analysed using a UV spectrophotometer at 261 nm to determine the amount of drug diffusion.[18] The cumulative percentage of drug release for the formulated products was presented in Table 6, alongside a graph depicting the relationship between time in seconds and the percentage of drug release, as illustrated in Figure 8.

Table 4: FTIR spectral data of DOXS, PVA, mixture of DOXS and PVA and optimized formulation.

Functional group	Standard wave no. cm^{-1}	DOX pure drug cm^{-1}	PVA polymer cm^{-1}	Mixture of drug and polymer cm^{-1}	Optimized formulation OF1 cm^{-1}
O-H	3050-3350	-	3308.76	3059.23	3319.49
$-CH_2$	2915-2940	-	2915.88	2938.68	2935.66
C=O	1650-1750	1717.24	1721.53	1726.36	1714.72
C-O	1050-1096	1092.92	1081.49	1096.58	1087.85
C-CH3 bending	1380-1458	1411.51	-	1446.67	1423.47
C=N	1550-1650	1582.95	-	1567.23	1649.14
C-O-C	1000-1310	1305.79	-	1297.18	1232.51

Table 5: Results of evaluations of formulated Doxylamine succinate FDBF.

Formulation code	Weight variation in mg	Folding endurance	Surface pH	Thickness in mm	% Moisture loss	Drug content in %
F1	82±3.05	183±2.0	6-7	0.23 ±0.05	0.48±0.01	95.27±0.16
F2	75±2.0	176±2.516	6-7	0.216 ±0.07	1.33±0.04	96.48±0.12
F3	60±3.0	132±2.00	6-7	0.17±0.07	0.83±0.01	87.39±0.24
F4	67.6±1.52	156±2.516	6-7	0.21±0.03	2.3±0.02	92.54±0.18
F5	57.66±1.5	198±2.60	6-7	0.143± 0.03	0.3±0.02	101.81±0.14
F6	63±2.30	148±3.0	6-7	0.19 ±0.05	1.90±0.04	86.48±0.20
F7	141.3±1.5	201±2.516	6-7	0.266± 0.04	1.13±0.01	98.60±0.25
F8	126.6±1.7	108±2.60	6-7	0.25 ±0.05	2.35±0.04	87.09±0.18

*Mean± SD *n*=3.

Table 6: Results of disintegration time and cumulative drug release of formulated Doxylamine succinate FDBF.

Formulation code	Disintegration time in sec	Cumulative drug release in %
F1	98±1.1	65.6%
F2	70±1.34	75%
F3	112±1.40	61.8%
F4	33±1.20	81%
F5	16±1.0	83.3%
F6	87±2.01	73%
F7	128±0.08	56%
F8	56±1.02	79.3%

*Mean± SD *n*=3.

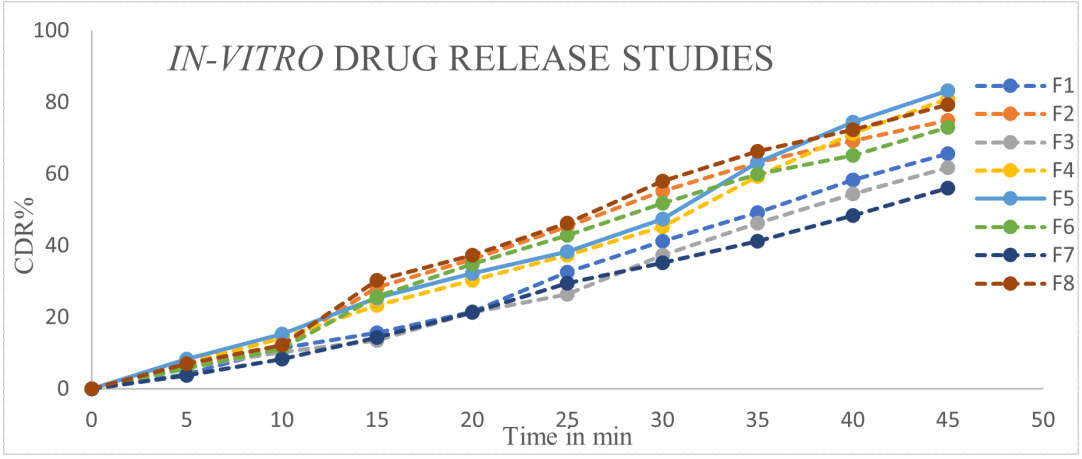

Figure 8: Cumulative drug release of Doxylamine succinate FDBF formulations F1-F8.

Statistical Analysis

Effect of formulation variable on disintegration time

The polynomial equation derived from the coded factors for response 1, which is disintegration time in seconds, is given below:

Y1=+75.00+31.25*X1+16.50*X2+7.25*X3

The statistical analysis revealed a significant model with a *p*-value of 0.0019, indicating its relevance. Moreover, individual factors-concentration of polymer 1 (X1), polymer 2 (X2) and plasticizer (X3)-were also statistically significant with *p*-values <0.05. The regression co-efficient for the response Y1 was found

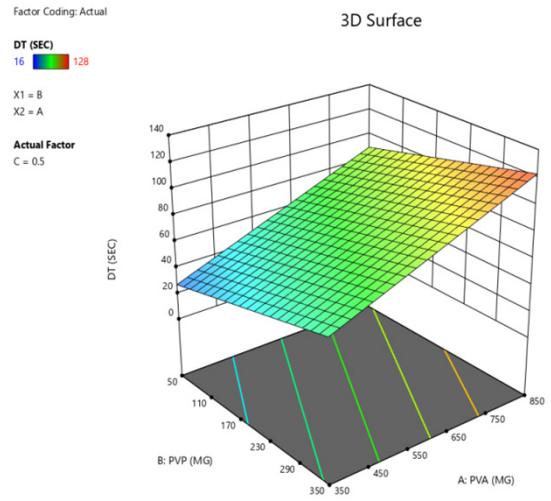

Figure 9: 3D Surface Plot influence of polymer on disintegration time.

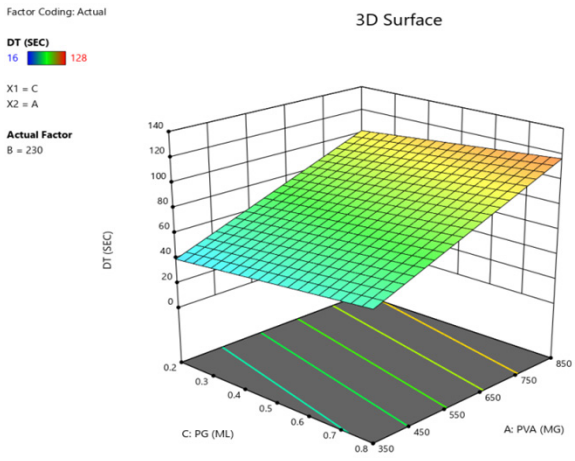

Figure 10: 3D influence of polymer and plasticizer on disintegration time.

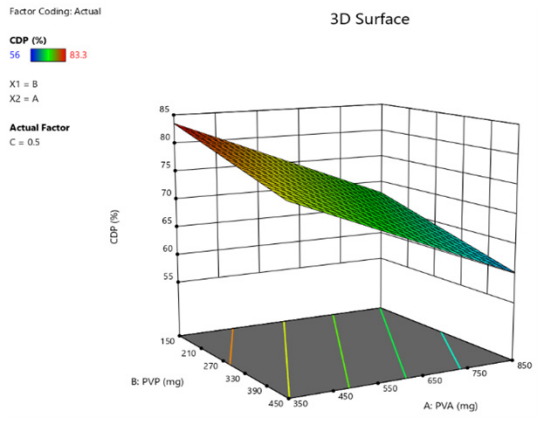

Figure 11: 3D Surface plot influence of polymer on CDR.

to be 0.9932 and statistics analysis summary is detailed in Table 7. The response surface plots Figures 9 and 10 illustrate the impact of these independent variables on the disintegration time. So, as

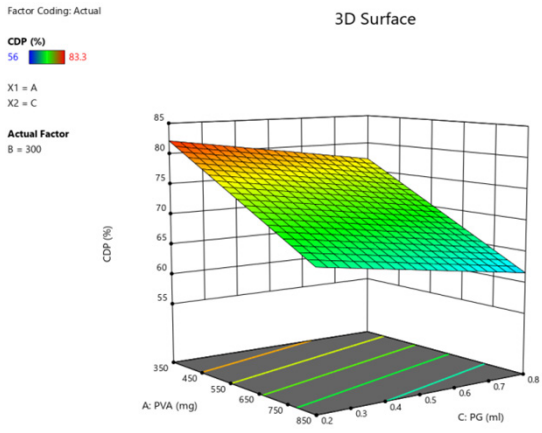

Figure 12: 3D Surface plot influence of polymer and plasticizer on CDR.

the concentrations of PVA and PVP increased, the disintegration time of the films also increased. Among these, PVA exhibited a more pronounced effect compared to PVP. Similarly, elevating the concentrations of PG and PVA led to an increase in the disintegration time of the films.[6]

Effect of formulation variable on cumulative drug release

The polynomial equation derived from the coded factors for response 2, which is cumulative drug release in % is given below:

Y2=+71.87-47.78*X1-3.85*X2-2.47*X3The statistical analysis confirmed the significance of the drug release model, given its *p*-value <0.05. Notably, the terms X1, X2, X3 were all deemed significant for Y2, with *p*-values <0.05. The regression co-efficient for the response Y1 was found to be 0.9678 and statistics analysis summary is detailed in Table 7. In equation Y2, the factors X1, X2 and X3 showed an antagonistic impact on drug release, as suggested by their negative coefficients (-47.78, -3.85 and -2.47, respectively). The response surface plots Figures 11 and 12 depict the impact of these independent variables on drug release. Particularly, PVA, recognized for its hydrophilic properties in regulating drug release, played a crucial role. Drug release from the films decreased with rising concentrations of both PVA and PVP. Additionally, increasing PG concentration alongside PVA led to reduced drug release from the films. Therefore, an optimal combination featuring lower concentrations of polymer and plasticizer would be preferable to enhance drug release from the films.[6]

OptimizationThe Design Expert software offers an optimization feature allowing users to set desired goals for factors and responses in their formulation. In this study, the aim was to minimize disintegration time while maximizing drug release within specified ranges for the FDBF. Using these goals, the software generated several solutions with desirability scores ranging from zero to one. Among these solutions, one formulation labelled OF1 stood out with a desirability of 0.981. This formulation was

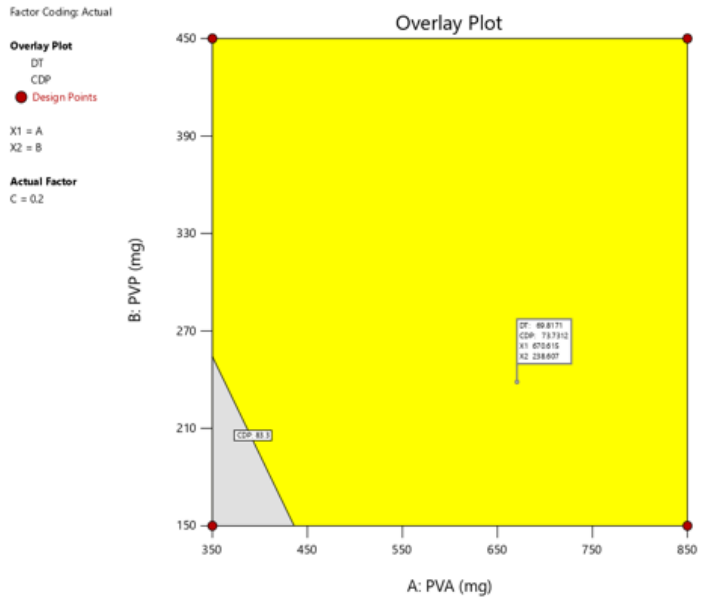

Figure 13: Design space of optimized OF1 formulation.

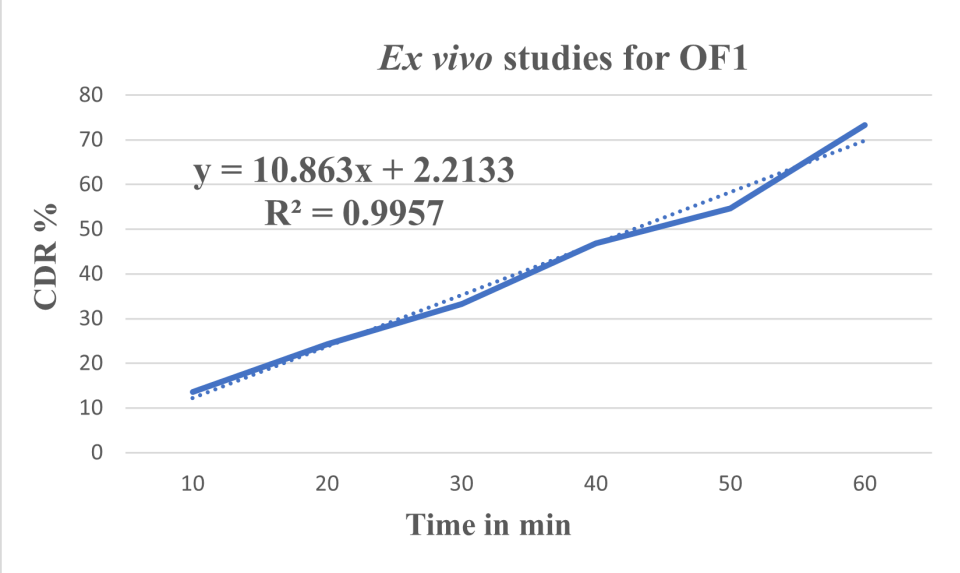

Figure 14: Cumulative drug release of optimized OF1 formulation.

predicted to achieve a disintegration time of 69.8 sec and a drug release of 73.72% as shown in Figure 13. Consequently, DP1 was selected and its performance closely matched the software's predictions, fulfilling all the optimization objectives.

Ex vivo StudyIn the diffusion cell setup, the mucosal surface was positioned facing the donor compartment, while the receptor compartment contained 13 mL of simulated saliva as the diffusion medium. The buccal film, sized at 1.5 × 1.5 cm^2, was placed in the donor compartment. The setup was fixed onto a hot plate magnetic stirrer, with continuous stirring of the solution in the receptor compartment at 100 rpm using magnetic beads, maintaining a temperature of 37±1°C. At predetermined intervals, specific volumes (0.6 mL) of the receptor fluid were withdrawn and promptly replaced with an equal volume of fresh diffusion medium. The samples underwent analysis for drug content at a wavelength of 261 nm using a double-beam UV spectrophotometer (UV-1900i Shimadzu). The optimized formulation OF1 was subjected to this procedure, the results of which are illustrated in Figure 14. The film exhibited 73.3% drug permeation within 60 min.[5]

Stability studiesThe stability study was conducted following the ICH guidelines, indicating no significant changes in the properties of the optimized formulation OF1 and drug release. Short-term stability assessments were carried out in a Stability chamber for 1 month on optimized fast-dissolving buccal film. Adequate samples were packed in stability containers and stored

Table 7: Model summary statistics of ANOVA analysis.

Response	*p* value	R^2	Adjusted R^2	Predicted R^2	Adequate precision	SD	CV%
Y1	0.001	0.9932	0.98801	0.9729	36.9240	4.21	5.62
Y2	0.0019	0.9678	0.9437	0.8712	17.1362	2.33	3.24

Table 8: Stability test results for Optimized formulation OF1.

Evaluation parameter at 30°C±2C and 65%±5% Relative Humidity (RH).			
Testing	**0 day**	**15 days**	**30 days**
Weight variation in mg	58.66±1.5	57.92±1.5	57.10±1.5
Thickness in mm	0.143±0.03	0.143±0.03	0.140±0.03
Drug content in %	97.46	96.53	95.18
% moisture loss	1.44±0.04	1.41±0.04	1.37±0.04
Disintegration time in sec	68	65	61
CDR in %	71.5	70.6	69.8

in the chamber at 30°C±2C and 65%±5% Relative Humidity (RH). Samples were withdrawn on 15th and 30th day for drug content estimation, thickness, weight, folding endurance and *in vitro* disintegration studies to determine drug release profiles. Results are detailed in Table 8.[16]

DISCUSSION

Doxylamine succinate was successfully designed, formulated and evaluated to enhance bioavailability and permeability, providing rapid relief from sudden allergic reactions by Design of Experiment (DOE) version 13. Fast-Dissolving Films (FDFs) containing Doxylamine succinate were prepared using the solvent casting technique. Various batches were formulated using the synthetic polymer PVA. The maximum absorption was observed at 261 nm with a pH 6.8 buffer solution and Beer's ranged from 10 to 60 µg/mL. An equation of y=m x+c was obtained, having a regression of 0.9978. The DSC thermogram showed that the peak temperature of pure Doxylamine succinate was recorded at 106.78°C. FTIR analysis of the physical mixture of the drug and polymer, the pure drug and the freshly prepared optimized formulation using both polymers indicated no significant chemical interactions between the drug and the excipients. The films demonstrated desirable properties in terms of thickness, weight variation, folding endurance, percentage moisture loss, surface pH, disintegration time and cumulative drug release, indicating they are compact, uniformly massed and durable during handling. The optimized formulation OF1 exhibited disintegration times of 68 sec with cumulative drug release rates of 71.5%. The *ex vivo* studies of OF1 films, formulated with both synthetic and natural polymers, demonstrated drug permeation rates of 73.3% within 60 min. The results of the short-term stability test of the optimized formulation OF1 of both polymers were done according to the International Council for Harmonization guidelines, confirming that the product stays stable for one month at a temperature of 30°C±2°C and relative humidity of 65%±5%. Based on these results, it can be concluded that FDBF presents a promising drug delivery approach for DOXS, bypassing first-pass metabolism. This facilitates rapid drug permeation, improving the absorption and bioavailability of the FDBF.

CONCLUSION

In this research, employing the Design of the Experiment facilitated the identification of how formulation variables affect FDBF performance. The developed films displayed favorable attributes: they were uniform, non-tacky, transparent and easy to remove. It was observed that the formulation variables, particularly the concentrations of PVA, PVP and PG, influenced both the drug release and disintegration time from the films. After optimization, formulation OF1 emerged as the optimal choice, promoting a disintegration time of 68 sec and a cumulative drug release of 71.5%. FDBF of DOXS can be an effective dosage form that provides rapid onset of action and relief from allergic reactions.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

DOXS: Doxylamine succinate; **FDBF:** Fast dissolving buccal films; **PVA:** Polyvinyl Alcohol; **PVP:** Polyvinylpyrrolidone; **v/s:** Versus; **PG:** Propylene glycol; **CDR:** Cumulative drug release.

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