RESEARCH PAPER

DESIGN AND OPTIMIZATION OF PROCHLORPERAZINE LOADED MICROSPONGES

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ABSTRACT

Aim of present work was to prepare and evaluate Sustained release microsponges of Prochlorperazine.The goal of the current study was to use the Quassi Emulsion Solvent Diffusion method to create prochlorperazine sustained release microsponges with various polymer ratios. FTIR was used to conduct drug-excipient compatibility investigations. Based on production yield, entrapment efficiency, and an in vitro release investigation, the optimal Microsponges formulation was identified. FTIR, DSC, and SEM analyses were performed on an optimized batch of microspheres. Several release kinetic models were fitted to the drug release data of the optimized batch. For a month, the improved batch of microsponges underwent a short-term stability investigation at 40 ± 2°C and 75% relative humidity.The medication and excipients did not interact. The Quassi Emulsion Solvent Diffusion Method was used to create the microsponges. The Higuchi model is followed by the medication release from the optimized microsphere formulation (B2). Optimized microsponges were spherical, according to SEM investigations.A stability investigation demonstrated the stability of the optimized formulation.Drug: The percentage of entrapment efficiency and drug release were significantly impacted by the polymer ratio and volume of Eudragit RS 100. Microsponges were found to be spherical in the Scanning Electron Microscopy (SEM) investigation. Following the stability trial, microspheres showed nearly identical medication release and no physical alterations. The optimized formulation was therefore stable.

Keywords: Prochlorperazine, Sustained release, Carbopol 974, Eudragit RS100, Quassi Emulsion Solvent Diffusion Method.

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INTRODUCTION

Sustained delivery systems seek to either reduce the frequency of dosage or improve the efficacy of the medication by localizing the drug to the site of action, reducing the necessary dose, or guaranteeing consistent drug delivery. Consequently, a sustained release dosage form is one that releases one or more drugs systemically over a predetermined period of time or constantly in a predetermined manner to a particular target organ.[1] Sustained release dosage forms provide better control of plasma drug levels, less frequent dosing, fewer side effects, increased efficacy, and reliable administration.[2]Furthermore, these systems may regulate the drug's release in the body either geographically, temporally, or both, and they provide a steady release of the medication over an extended period of time. To put it another way, the system works well to maintain consistent medication levels in the target tissue or cells. A gradual release over an extended period of time, followed by an initial release soon after administration, is referred to as sustained release.[3] Microsponge Delivery Systems (MDS) are highly cross-linked, porous polymeric microsponges that may absorb a range of active chemicals and release them gradually.

2. MATERIALSANDMETHODS

2.1 Materials

Vaikunth Chemicals, Ankleshwar, Gujarat India, Ltd. provided a gift sample of prochlorperazine, while Signet Chemical Co., India, sent a gift sample of eudragit RS. The remaining ingredients were all of analytical quality.

2.2 Method of Preparation

Preparation of microsponges by Quassi Emulsion Solvent Diffusion Method

The medication and Eudragit RS 100 + Carbopol 974 were distributed using dichloromethane. The organic phase was added to the external phase, which often contains a stabilizer such polyvinyl alcohol. At this stage, glycerol was introduced to promote plasticity.

After emulsification, the system was continuously stirred for two hours. When the internal phase is mixed with the exterior medium, a microsponge is produced.After that, the mixture was filtered to remove the Microsponge. After cleaning, the microsponge was left to dry at room temperature. [4]. Different amounts of Eudragit RS 100 were utilized, and different batches of microsponge were produced.

2. EVALUATION STUDY

Preformulation Parameters

Drug's initial characteristics can be used to identify a specific material. The physicochemical properties of prochlorperazine were investigated. i) Color ii) Smell

Solubility study of drug

The drug solubility study employed water and a number of buffer solutions with pH values between 1.2 and 6.8. An excessive amount of medication was added to the buffer solution to produce the saturated solution.Three ten-minute sonications of saturated solutions were then carried out. The produced solutions were filtered using Whatman filter paper. Spectrophotometric examination of the filtrate at 294 nm was performed using the same medium as the blank. The amount of medication dissolved was measured using the calibration curve.

Identification of drug by FTIR

The FTIR studies were carried out utilizing the pressed pellet method with a KBr press. The KBr was put in a hot air oven for two hours to eliminate any remaining moisture. Medication pellets and an optimized batch of microsponges were made using the previously indicated dried KBr. The generated pellet was scanned in the 400–4000 cm-1 wave number range while being kept in the instrument's sample holder. After that, the final finger print was contrasted with the reference standard.[6]

Flow properties

The flow characteristics of the Prochlorperazine Microsponges powder sample, including bulk density, tapered density, Carr's index, Hausner's ratio, and angle of repose, were assessed [7].

3. FORMULATION PARAMETERS

Flow Properties

All prepared microsponges were evaluated for their flow properties.

Particle Size Analysis

The particle size distributions of the microsponges are ascertained by optical microscopy using a calibrated ocular lens. A compound microscope is used to study a smear of the product distributed in light liquid paraffin. Each time, a calibrated eyepiece is used to measure the size of 100 microsponges in micrometers.

% Practical yield

The yield of microsponges was determined by comparing the total weight of the microsponges generated to the total weight of the copolymer and medicine. The practical yield is calculated by dividing the mass of microsponges acquired by the total weight of the drug and poly microsponges produced, rather than the total weight of the copolymer and drug [8].

Drug entrapment efficiency

Microsponges containing 20 mg of the drug were ingested for assessment. The amount of drug entrapped was determined by repeatedly crushing the microsponges and extracting with aliquots of 6.8 phosphate buffer. After the extract was transferred to a 100 ml volumetric flask, the volume was adjusted using 6.8 PB. Following the proper dilution, the solution was filtered, and using 6.8 phosphate buffer as a blank, the absorbance was measured spectrophotometrically at 294 nm. The percentage of medicine trapped in the microsponges was calculated using the formula below:

Drug Entrapment = (Theoretical Drug Content/Calculated Drug Content) x 100

The following formula was used to determine drug loading: %Drug Loading = (Drug Weight in Microsponges/Microsponges Weight) x 100

***In vitro* drug release studies**

In vitro drug release studies were conducted using USP dissolution test equipment (Type 1). The apH progression method was used to conduct the dissolving studies in 900 cc of dissolution media that was stirred at 37±0.5°C and 50 rpm. For example, pH 6.8 for the remainder research and pH 1.2 for the first two hours. Aliquots were taken out and replaced with fresh media on a regular basis. Aliquots were taken out and replaced with fresh media on a regular basis.[9]

Release Kinetics

The release data is analyzed using the following mathematical models to investigate how drugs are released from microsponges: zero-order, first-order, and Higuchi and Korsmeyer Poppas' model investigations. Aliquots were taken out and replaced with fresh media on a regular basis.

Optimization of microsponges by using 3^2factorial design method

For the purpose of optimization,

X_1=Concentration of Eudragit RS100(%)

X_2= Concentration of Carbopol 974(%)

Y_1=Entrapment Efficiency(%)

Y2= Drug release (%) [10,11]

Characterization of optimized batch of microsponges by using different techniques

FTIR: Prepared Optimized batch of microsponges were characterized by FTIR as described

Scanning electron microscopy

The surface structure of microsponges was examined using scanning electron microscopy (SEM-JSM 5000). SEM images were taken at the required magnification after the generated microsponges were

coated with gold palladium at room temperature in an argon atmosphere.

Stability Study

Batch B2 of manufactured microsponges underwent a stability investigation in accordance with ICH guidelines. They were kept in a stability chamber for 30 days at 40 ±2°C and 75% relative humidity. The optimized batch of microsponges was contained in USP type-1 flint vials that were hermetically sealed with bromo butyl rubber plugs and aluminum lids.The entrapment efficacy and drug release of the formulation were evaluated after a month.[12, 13, 14, 15, 16].

Table 1. Optimization using factorial design method

Variables	-1	0	+1	Responses
X1=Concentration of Eudragit Rs100 (%)	400	500	600	Y1=Entrapment Efficiency (%)
X2=Concentration of Carbopol 974(%)	200	250	300	Y2=Drug release (%)

4. RESULTS AND DISCUSSION

Preformulation Studies

Organoleptic properties

Table 2.Organoleptic properties of Prochlorperazine

Properties	Results
Description	White Crystalline Powder
Odor	Odorless
Color	White
State	Solid

Identification of drug by FTIR

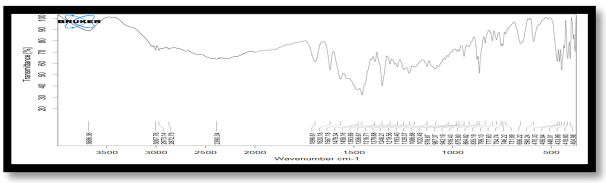

Fig.1.FTIRof Prochlorperazine

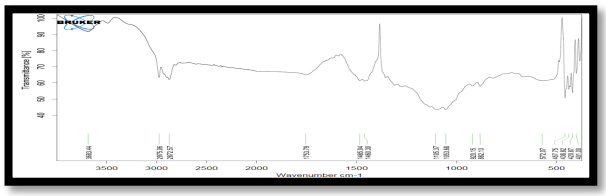

Fig.2.FTIR spectra of physical mixture of Eudragit RS 100

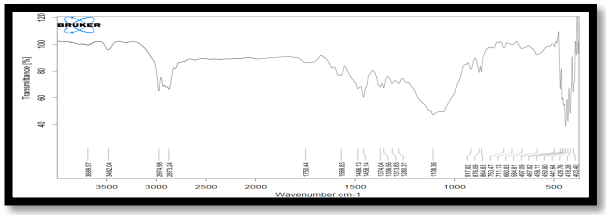

Fig.3.FTIR spectra of physical mixture of Drug+ Mixture

Interpretation

Table 3.Interpretation of FTIR graphs

Sr No.	Functional Group	Wave No. (cm^{-1})	
		Reported Value	Observed Value
1)	C-S	1200-1280	1279.68
2)	C-N amine	1300-1350	1316.71
3)	C=C	142	1458.1

	(aromatic)	0-1600	6 and 1567.18
4)	CH (aromatic)	2900-3000	2973.14

Table 4: Physical properties of drug

Experiment	Properties	Observations
Physico-mechanical properties	Bulkdensity	3 0.27±0.0057g/cm
	Tappeddensity	3 0.483±0.028g/cm
	Hausner'sratio	1.36±0.577
	Angleof repose	19.11
	Compressibilityindex	29.6±0.57 %
	MeltingPoint	217.39ºC
Solubility(mg/ml)	Water	0.011±0.16
	0.1NHCl	**11±0.12**

Formulation Parameters

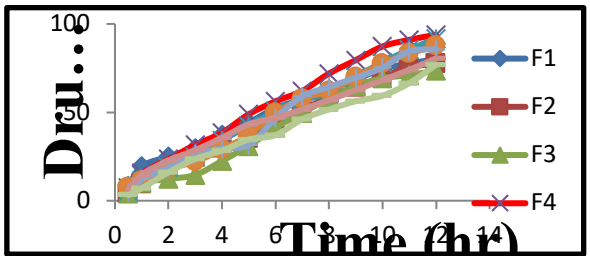

Fig 4 *In-vitro* drug releases study

From the above evaluation study, it was concluded that with increase in Eudragit RS100, concentrations, sustained release pattern was obtained.

Table 5 Release kinetic profile of optimized batch

Optimized formulation	Higuchi (R^2)	Zero order (R^2)	First order (R^2)	Korsmeyer peppas (R^2)
F4	0.9	0.5	0.8	0.9

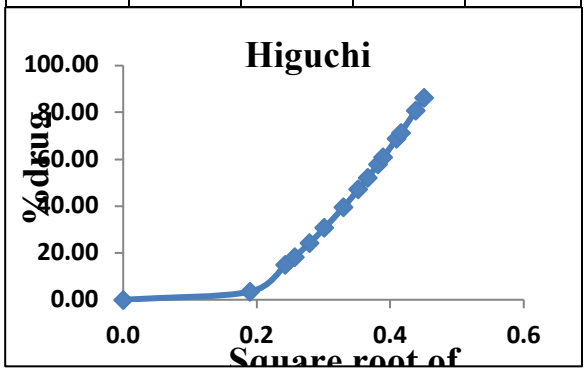

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Fig 5 Release Kinetics

According to the higuchi model formulation followed first burst release and then gives the sustained release effect.

Optimization of microsponges by using 3^2 factorial design method

Layout of optimization (A)

Variables		-1	0	+1	Responses
X1=Concentration of Eudragit	Numeric	1	2	3	Y1=Entrapment Efficienc

Rs100(%)				y (%)
X2=Concentration of Carbpol 974(%)	Numeric	2.5	7.5	Y2=Drugrelease (%)

Table 6 Layout of optimization (B)

Run	Coded Value		Actual Value	
Batch Code	**X1**	**X2**	**X1**	**X2**
B1	-1	-1	1	2.5
B2	0	-1	2	2.5
B3	+1	-1	3	2.5
B4	-1	0	1	5
B5	0	0	2	5
B6	+1	0	3	5
B7	-1	+1	1	7.5
B8	0	+1	2	7.5
B9	+1	+1	3	7.5

ANOVA for % entrapment efficiency(responseY1)

Table 8. ANOVA table for response Y1:Entrapment Efficiency

Source	Sum of square	df	Mean square	F-value	P-value	
Model	82.25	2	41.12	20.92	0.0020	Significant
A-EudragitRs100	48.17	1	48.17	24.50	0.0026	
B-$CaCl_2$	34.08	1	34.08	17.34	0.0059	
Residual	11.79	6	1.97			
Cor Total	94.04	8				

Contour plot of % entrapment efficiency(response Y1)

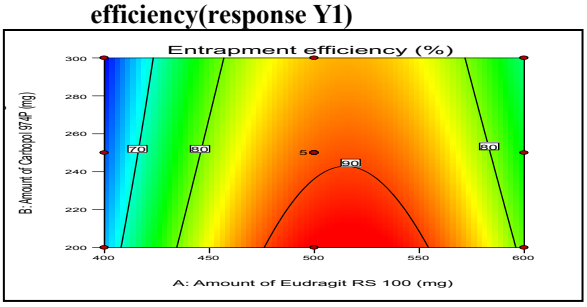


Fig.6.Contour plot showing the effect of Eudragit RS100(X1) and $CaCl_2$(X2) on response Y1 (% Entrapment Efficiency)

Response surface plot of % entrapment efficiency(responseY1)

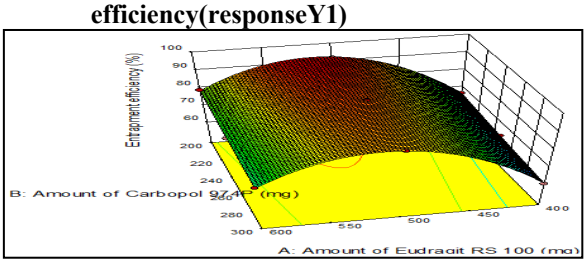


Fig.7.Response surface plot of % entrapment efficiency(ResponseY1)

ANOVA for % CDR (responseY2)

Table 9. ANOVAtablefor%CDR(responseY2)

Source	Sum of square	Df	Mean square	F-value	P-value	
Model	256.70	2	128.35	23.46	0.0015	Significant
A-EudragitRs100	178.21	1	178.21	32.57	0.0013	
B-$CaCl_2$	78.48	1	78.48	14.35	0.0091	
Residual	32.83	6	5.47			
Cor Total	289.52	8				

Counter plot of % drug release(response Y2)

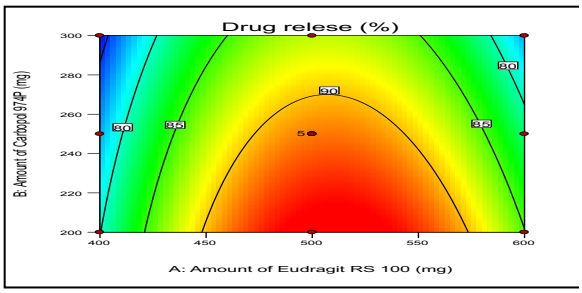


Fig.8.Contour plot showing the effect of Eudragit RS100(X1) and Carbopol 974(X2) on responseY2 (% Drug release)

Response surface plot of % Drug release(Response Y2)

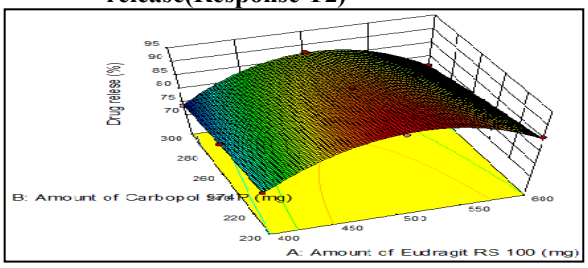


Fig.9.Response surface plot of %drug release(Response Y2)

Overlay plot

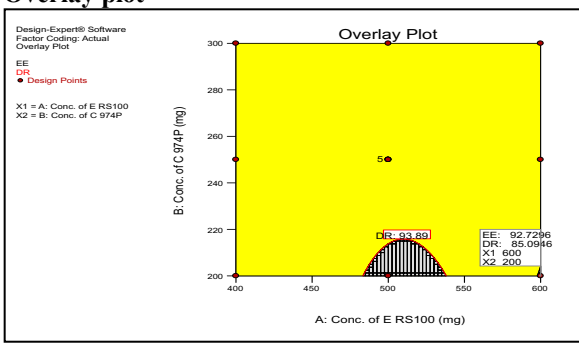


Fig.10.Ovelay plot of Eudragit RS100 & Carbopol 974

Table 10. Suggested solution formula given by the design expert

Name	Goal	Lower Limit	Upper Limit
X_1=Amount of Eudragit RS 100 (mg)	In range	400	600
X_2=Amount of Carbopol 974P (mg)	In range	200	300
Y_1=Entrapment efficiency (%)	Maximize	60.23	92.14
Y_2=Drug release (%)	Maximize	73.7	93.89

Table 11. Predicted&observedvaluesofcheckpointbatchB2

Name	X_1	X_2C	Response	Predicted	Observed	% Error
M_1	553.7	200	Y_1(Entrapment efficiency) (%)	92.94	93.05	0.118
			Y_2 (% Drug release)	92.69	93.02	0.508

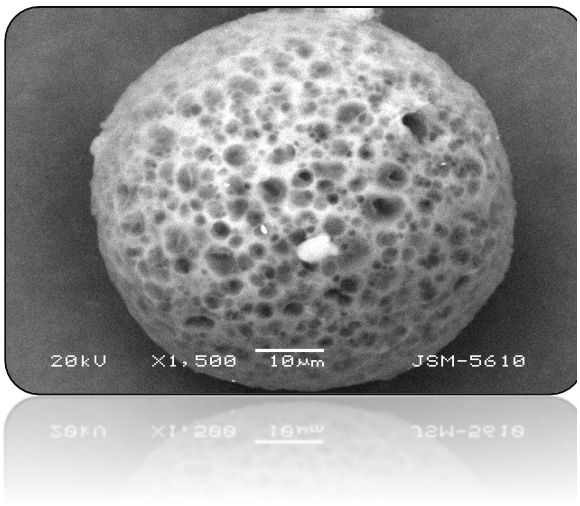
Predicted error (%) = (observed value − predicted value)/predicted value × 100%

Characterization of Optimized Batch of Microsponges by using DifferentTechniques

FTIR of optimized batch of microsponges

Fig.11.FTIR spectra of optimized batchB2

Scanning Electron Microscopy of optimized batch



From the above figure it was observed that microsponges were spherical in shape

Fig.12 SEM of optimized batch

Stability Study

Short term stability conditions of temperature and relative humidity (45 ± 2°C/75% ± 5% RH).

Table 12.Characterizationof optimized Batch after stability

Parameters	Initial	After1month
Particle size	52.89 µm	50.69
%Entrapment Efficiency	79.56	79.06
% CDR	86.12	85.41

Table15.Characterizationof optimized Batch after stability

From the above results it has been observed that the formulation showed no significant change in appearance, particle size, % entrapment efficiency, % drug release. So, the prepared formulation was found to stable at accelerated.

5. CONCLUSION

For this study, sustained release microsponges that hold the formulation for a long period were created.Microsponges were made using the Quassi Emulsion Solvent Diffusion Method.Several factors, such as drug release, trapping effectiveness, and production yield, were taken into consideration when creating the microsponges. Pre-formulation studies were carried out to confirm that the drug and polymer were compatible. SEM examinations revealed that microsponges were spherical in form. To determine how temperature and humidity affected the percentage of entrapment efficiency and drug release, stability tests were carried out for a month at 40 ± 2°C and 75% relative humidity. The modified formulation's entrapment efficiency and in vitro release studies did not significantly change, according to the stability trials, suggesting that the formulation is stable.

6. CONSENT

Not applicable

7. ETHICAL APPROVAL

Not applicable.

8. COMPETING INTERESTS

Authors have declared that no competing interests exist.

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