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DESIGN, FORMULATION, AND EVALUATION OF RISPERIDONE MUCOADHESIVE BUCCAL PATCHES

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Abstract

Objectives: To construct and optimize Risperidone (RIS) mucoadhesive buccal films for systemic distribution as an alternate route. To make buccal patches of Risperidone utilizing natural polymers such sodium alginate (SA), Hydroxypropyl methylcellulose (HPMC), Na CMC, and Carbopol 934 (CP 934).

Method: Solvent casting created Risperidone buccal patches. The optimization study used a software-based response surface methodology approach with 2^3 factorial designs to evaluate 8 formulations of Risperidone mucoadhesive buccal patches to determine the significant effect of selected independent variables on the dependent variable. To assess patch appearance, thickness, weight homogeneity, folding durability, medication content, surface pH, swelling index, and FTIR. Invitro dissolution, ex-vivo permeation, residence time, and stability tests.

Results: FTIR and DSC showed that Risperidone was entirely entrapped in polymer carrier bonds with no chemical interaction. Drug distribution was uniform in buccal patches at 90.14± 0.07 and 98.75± 0.80.

Conclusion: Buccal patch medicine release and penetration depended on polymer type. Hydrophilic polymers boosted buccal patch drug release. F6 was the best of F1–F8. Formulation F6 had 82.03 ±0.82% in-vitro drug release and 75.21 ± 0.42% ex-vivo permeability after 7 hours. Stability tests did not modify appearance, surface pH, content homogeneity, in-vitro residence length, medication release, or ex-vivo penetration.

Keywords: Mucoadhesive buccal films, Risperidone, Hydroxypropyl methylcellulose,Sodium Carboxyl methyl cellulose, and Carbopol 934.

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1. Introduction

The buccal route as an alternative to other traditional method of systemic drug administration is a subject of growing interest because of numerous advantages. It is well known that the absorption of therapeutic compound from the oral mucosa provide a direct entry of the drug into the systemic circulation, therefore avoiding the first pass hepatic metabolism and gastrointestinal drug degradation which is associated with oral administration [1]. The oral cavity is easily accessible for self-medication and hence it is well accepted by patient, and it is safe since the device can be easily administered and even removed from the site of application, stopping the input of drug whenever desired [2].

Drug like Risperidone has been selected as model drug because the drug has all the pharmacokinetics and physico-chemical properties required for controlled release. Risperidone has oral bioavailability 70 % and having elimination half-life of 20 hrs and having volume of distribution 1 to 2 L/kg. The Risperidone is freely soluble in water [3].

Therefore, in the present study an attempt will be made to formulate buccal dosage form of Risperidone using different polymers and adjuvants to avoid hepatic first pass metabolism.

2. Materials and Methods

Risperidone was obtained as gift sample from APEX pharmaceutical limited, Chennai. Sodium alginate, Sodium

carboxymethyl cellulose, HPMC, Carbopol 934 was procured from Bross chemicals Tirupati. All other solvents were used as analytical grade purpose

2.1. Design of an Experiment

The experimental design employed in this study was a 23 factorial design, with the quantity of HPMC labelled X1, quantity of CP 934 labelled X2, and the quantity of Na CMC labelled X3 and they are presented in Table 1. The 2 levels chosen for both X1, X2, and X3 in the case of X1, were coded as -1=100 mg and +1=300 mg. X2 was coded as -1 = 100 mg and +1 = 300 mg. X3 was coded as -1 = 100 mg and +1 = 300 mg. In Table 2, the factorial trail formulations are presented.

2.2. Formulation Design of mucoadhesive buccal patches of Risperidone

A software-based response surface methodology approach using Design of Experiment (DOE-13), 23 factorial design, Quadratic mode 23 factorial design, was employed for the optimization study. In the current experimentation, three independent formulation variables were HPMC labelled X1, quantity of CP 934 labelled X2, and the quantity of Na CMC labelled X3 and the dependent variables selected were (Y1) % In-vitro drug release, (Y2) Ex-vivo permeation. Total 8 different formulations of mucoadhesive buccal patches of Risperidone were evaluated to determine the significant effect of selected independent variables on the dependent variable (Basak et al., 2006) [4-6].

Table.1: Layout for an experimental design

Factor	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)
X1- HPMC	+ (100)	+ (300)	-	-	+ (200)	+ (100)	+ (200)	+ (100)
X2- CP 934	-	-	+ (100)	+ (300)	+ (100)	+ (300)	-	-
X3- Na CMC	-	-	-	-	-	-	+ (100)	+ (300)

Table. 2:Composition of mucoadhesive buccal patches of Risperidone

Formulation	Risperidone(mg)	SA (mg)	HPMC (mg)	CP 934 (mg)	Na CMC (mg)	PropyleneGlycol %	DistilledWater (ml)
F1	50	900	100	-	-	10	40
F2	50	700	300	-	-	10	40
F3	50	900	-	100	-	10	40
F4	50	700	-	300	-	10	40
F5	50	700	200	100	-	10	40
F6	50	600	100	300	-	10	40
F7	50	700	200	-	100	10	40
F8	50	600	100	-	300	10	40

2.3. Preparation of mucoadhesive buccal patches by solvent casting method

The Buccal Patches were preferably formulated using the solvent casting method. Backing membrane was casted by pouring 4% w/v aqueous solution of PVA on aluminum foil in 9 cm petri dishes at 42°C and left for 10 h. Phosphate buffer saline, pH 6.8, was used as solvent in the casting method. A series of buccal patches composed of different ratios and combinations of polymers were prepared by solvent casting technique. Propylene glycol was incorporated as a plasticizer and penetration enhancer at a concentration of 10% w/w of dry weight of polymers. Fifty milligrams of Risperidone were incorporated in mixtures containing different ratios and combinations of polymers and plasticizer7. The matrices were prepared by pouring 40 ml of the homogeneous solutions on the PVA- aluminum foil backing membrane. Then, these buccal patches were dried at 42°C in an incubator. After 24 h, the dried patches were removed from the petri dishes and kept in desiccators until use [8].

2.4. Identification of drug

a) Identification by FTIR spectroscopy: Risperidone discs were prepared by pressing the Risperidone with potassium bromide and the spectra in between 4000 to 500 cm-1 was obtained under the operational conditions. The absorption maximums in spectrum obtained with the substance being examined correspond in position and relative intensity to those in the reference spectrum represented [9].

b) Identification by melting point: Melting point of the drug was determined by capillary tube method [10].

c). Organoleptic properties: The color, odour and taste of the drug were recorded using descriptive terminology [11].

d). Solubility study: It is important to know about solubility characteristic of a drug in aqueous system, since they must possess some limited aqueous solubility to elicit a therapeutic response. The solubility of drug was recorded by using various descriptive terminologies. The solubility profile was represented [12].

e) Determination of λmax: The absorption maximum of the standard solution was scanned between 200-400 nm regions on UV-Visible spectrophotometer. The absorption maximum obtained with the substance being examined corresponds in position and relative intensity to those in the reference spectrum [13].

f) Development of standard curve of Risperidone: Accurately weighed 50 mg of Risperidone, was dissolved in little quantity of pH 6.8 and volume was adjusted to 50 ml with the same to prepared standard solution having concentration of 1000 µg/ml. From that 1ml is pippeted out and makes upto 10ml to obtained a concentration of 100 µg/ml. From the stock solution, aliquots of 0 .5, 1, 1.5, 2 and 2.5 ml were transferred into 100 ml volumetric flasks and final volume was made upto 10 ml with pH 6.8. Absorbance values of these solutions were measured against blank (pH 6.8) at 271.5 nm using UV-Visible spectrophotometer [14].

2.5. Drug Excipient Interaction Studies

a) Fourier transform Infra-Red (FTIR) spectroscopy: FTIR study was carried out to check compatibility of drug with polymers. Fourier transform Infrared Spectrophotometer was determined by using KBr dispersion method. The base line correction was done using dried potassium bromide. Then the spectrum of dried mixture of Risperidone and potassium bromide was run followed by Risperidone with various polymers by using FTIR spectrophotometer. The absorption maximums in spectrum obtained with the substance being examined correspond in position and relative intensity to those in the reference spectrum was represented [15].

b) Differential scanning calorimetry (DSC): Any possible drug polymer interaction can be studied by thermal analysis. The DSC study was performed on pure Risperidone, Risperidone + HPMC, Risperidone + carbopol-934, Risperidone + sodium alginate and Risperidone + NaCMC. The 2 mg of sample were heated in a hermetically sealed aluminum pans in the temperature range of 25-300 ºC at heating rate of 10ºC /min under nitrogen flow of 30ml/min [16].

2.6. Evaluation of Risperidone Buccal patches

The Risperidone Buccal Patches were evaluated for the following properties:

2.6.1. Physical parameters

a) Physical appearance and surface texture of patch

This parameter was checked simply with visual inspection of patches and evaluation of texture by feel or touch [17].

b) Weight Uniformity of patches

Three patches of the size 29 mm diameters were weighed individually using digital balance and the average weights were calculated [18].

c) Thickness of patches

Thickness of the patches was measured using screw gauge with a least count of 0.01mm at different spots of the patches. The thickness was measured at three different spots of the patches and average was taken [19].

d) Folding Endurance of patches

The flexibility of patches can be measured quantitatively in terms of what is known as folding endurance. Folding endurance of the patches was determined by repeatedly folding a small strip of the patches (approximately 2x2 cm) at the same place till it broke. The number of times patches could be folded at the same place, without breaking gives the value of folding endurance [20].

e) Swelling Index of patches

The swelling Index of the patches determined by immersing pre weighed patch of size 29mm in 50 ml water. The strip was taken out carefully at 5 and10 min. intervals, blotted with filter paper and weighed accurately [21].

$$\% \text{ Swelling Index} = \frac{\text{Wet Weight} - \text{Dry Weight}}{\text{Wet Weight}} \times 100$$

f) Surface pH of patches

Surface pH was determined by the patches were allowed in contact with 1ml of distilled water. The surface pH was noted by bringing a combined glass electrode or pH paper near the surface of patches and allowing to equilibrate for 1 min [22].

2.6.2. Mechanical parameters

a) Invitro residence time

The *invitro* residence time was determined employing a modified USP disintegration apparatus. The disintegration medium was composed of 800 mlisotonic phosphate buffer of pH 6.8 (IPB) maintained at 37± 0.5 0C. A piece of porcine buccal tissue, 3 cm length was used for this study. The tissue was attached to a rectangular glass piece using cyanoacrylate adhesive from non-mucosal surface. The mucoadhesive patch was hydrated from one surface using pH 6.8 IPB and then the hydrated surface was brought into contact with the mucosal membrane. The glass slab was vertically fixed to the apparatus and allowed to move up and down so that the patch was completely immersed in the buffer solution at the lowest point and was out at the highest point. The time necessary for complete erosion or

detachment of the patch from the mucosal surface was observed and recorded (n=3) [23-25].

b) Invitro release study

The in vitro drug release studies were performed by using USP dissolution test apparatus (paddle method). A film of 29mm diameter size was cut and attached to a glass slide with a few drops of phosphate buffer (pH 6.8). This slide was kept at an angle of 45º in a 1000 ml beaker containing 250 ml of phosphate buffer pH 6.8 solutions. The dissolution medium was maintained at a temperature of 37 ± 0.5º C and stirred at 50 rpm. At predetermined time intervals samples were withdrawn and replaced with fresh dissolution medium. The samples were filtered through 0.45µm Whatman filter paper and made appropriate dilutions with phosphate buffer pH (6.8). Absorbance was measured using UV- VISIBLE spectrophotometer. Drug release and the cumulative percentage of drug released were determined [26-28].

c) Content Uniformity

Content uniformity was determined by dissolving one patch of 29mm diameter contain 5 mg of Risperidone in 10 ml of phosphate buffer solution (pH6.8). And the contents were stirred with the help of magnetic stirrer to dissolve the film. The contents of solution were transferred to a volumetric flask (10 ml). The absorbance of the solution was measured against the corresponding blank solution at 271 nm using UV spectrophotometer. The experiments were carried out in triplicate for each formulation and average value was calculated29-30.

d) Ex vivo permeation studies

Activation of cellophane was carried out by soaking the membrane for 10-12 h in buffer solution prior to use,

Permeation through cellophane membrane

Activated cellophane membrane was mounted to the donor compartment of the diffusion cell having a surface area of 5.065 cm2 and clamped with receptor compartment which was filled with PBS pH 6.8. The diffusion cell was placed on the magnetic stirrer and the temperature maintained at 37°C. One mg/ml of it drug solution continuously stirred at 37°C, removed at an appropriate interval for spectrophotometric determination and cell was immediately refilled with fresh receptor solution [31-32].

e) Stability Studies

In any rational drug design or evaluation of dosage forms, the stability of the active component was a major criterion in determining their acceptance or rejection. The formulation (F7) was stored at accelerated condition in aluminum foils for 3 months. The samples were withdrawn after end of 1st month, 2nd month and 3rd month. The samples were analyzed for its drug content and *invitro* drug release [33-36].

3. Results and Discussion

3.1. Identification of drug

a) Identification of drug by FTIR spectroscopy

The FTIR spectrum of Risperidone was shown in Figure1 and the interpretations of IR frequencies were represented. The major peaks are identical to functional group of Risperidone Hence; the sample was confirmed as Risperidone.

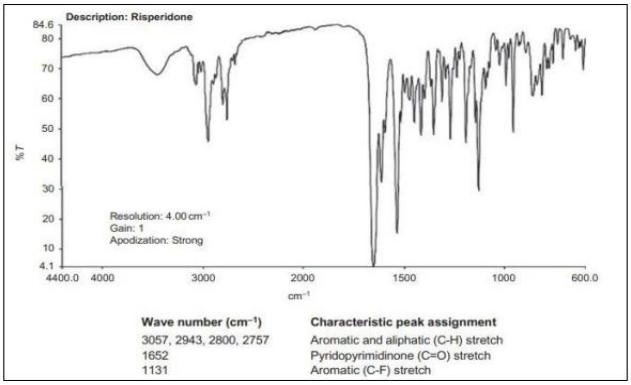


Figure. 1: FTIR spectrum of Risperidone

b) Melting point: The reported melting point for Risperidone was 170.0°C. Hence, experimental values were same as official values.

c) Organoleptic properties

Physical state: Fine powder
Colour: A white fine powder
Odour: Characteristic
Taste: Bitter to alkaline

d) Solubility study

Table. 3: Solubility of Risperidone in various solvents

Name of solvent	Standard Parts of solvent required for part of solute	Solubility
Distilled water	From 1 to 10	Freely Soluble
Methanol	From 10 to 30	Soluble
Isopropyl alcohol	From 100 to 1000	Slightly soluble
pH 6.8	From 10 to 30	Soluble
pH 7.4	From 10 to 30	Soluble

e) Determination of λmax

UV absorption spectrum of Risperidone in pH 6.8 (phosphate buffer) showed λ max at 271.5 nm was shown in figure 2. The graph of absorbance vs. concentration for Risperidone was found to be linear in the concentration range of 5– 25 µg/ml. The drug obeys Beer- Lambert's law in the range of 5–25 µ/ml was shown in figure 3.

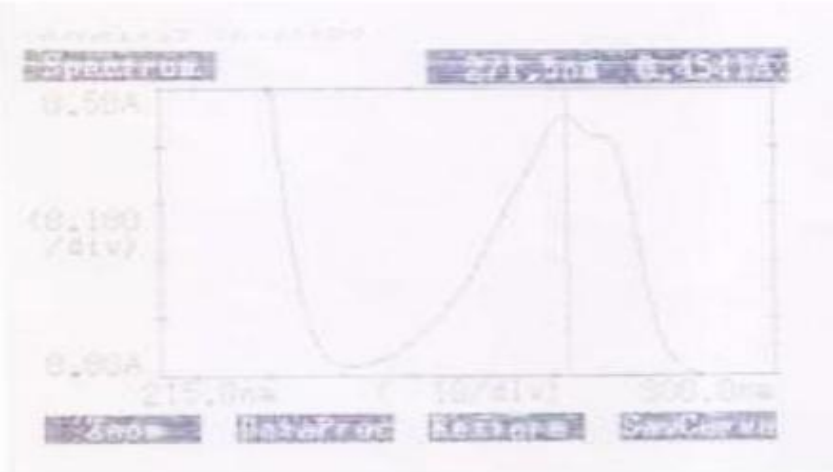


Figure. 2: λmax observed for Risperidone in pH 6.8 (Phosphate buffer)

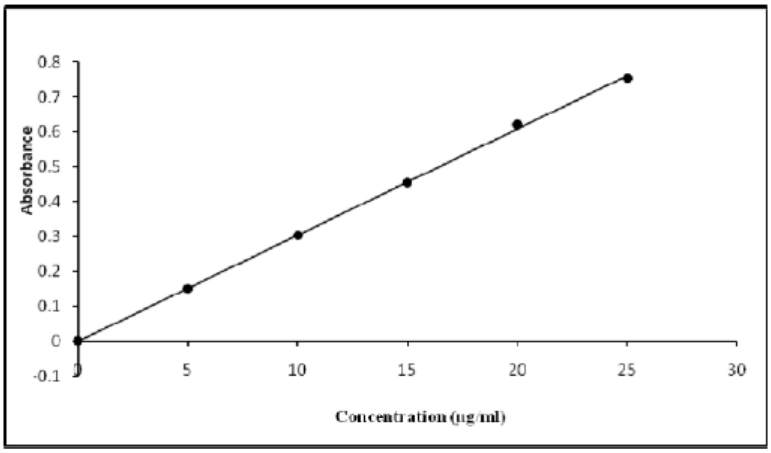


Figure. 3: Standard curve for Risperidone in pH 6.8

3.2. Drug Excipient Interaction Studies

a) Determination of compatibility for drug with polymer by FTIR spectroscopy

The major peaks of Risperidone spectrum were compared to Risperidone with polymers spectrum. There was no interaction between Risperidone and polymers. The peaks were represented in table 4and spectrums where shown in figure 4.

Table. 4: The FTIR spectrum of Risperidone and Risperidone with different polymers

W.No. (cm-1)	Functional group	RSP	RSP+SA	RSP+HPMC	RSP+CRB 934	RSP+Na CMC
3065-3057	Aromatic C-H Stretching	Yes	Yes	Yes	Yes	Yes
2943-2925	Aliphatic C-H Stretching	Yes	Yes	Yes	Yes	Yes
1652-1645	C-O Stretching	Yes	Yes	Yes	Yes	Yes
1131-1125	C-F Stretching	Yes	Yes	Yes	Yes	Yes
837-982	C-H bending	Yes	Yes	Yes	Yes	Yes

***RSP- Risperidone; SA-Sodium alginate; HPMC-Hydroxypropyl methylcellulose; CRB 934-Carbopol 934; Na CMC-Sodium Carboxymethyl Cellulose**

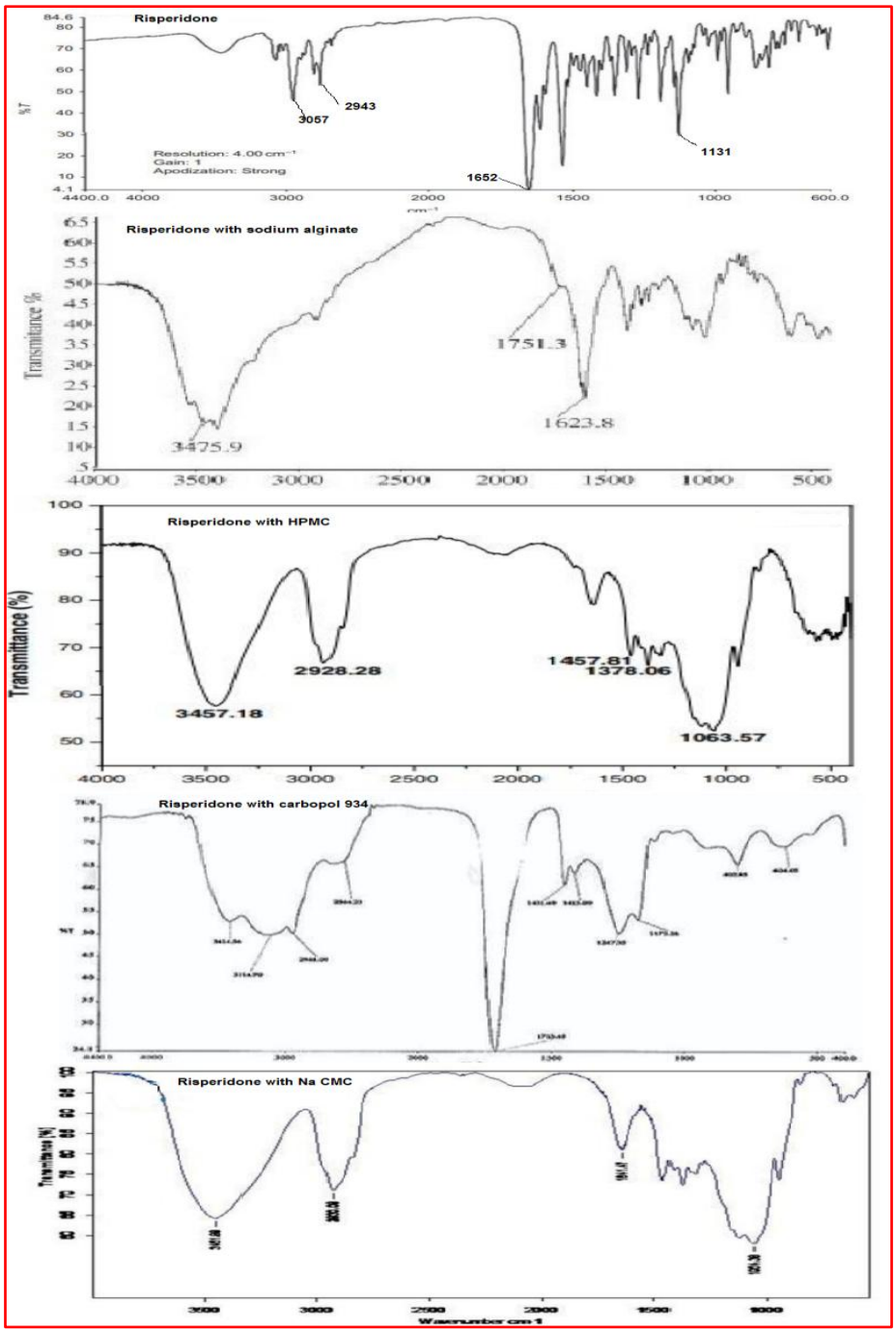


Figure. 4: FTIR spectrum of Risperidone and Risperidone with different polymers used in formulations.

b) DSC thermal analysis

The interactions between Risperidone and polymers were determined by DSC studies and results were represented in Table 5 and Thermogram curves where shown in Figure 5.

Table. 5: Various DSC thermogram parameter

S. No.	DSC of Substance	Peak (°C)	Onset temperature (°C)	End set temperature (°C)
1	Risperidone	182.19	167.63	190.01
2	Risperidone + sodiumalginate	181.38	170.30	185.81
3	Risperidone + carbopol934	180.83	169.01	186.93
4	Risperidone + HPMC	180.70	171.80	184.38
5	Risperidone + Na CMC	180.83	169.01	187.93

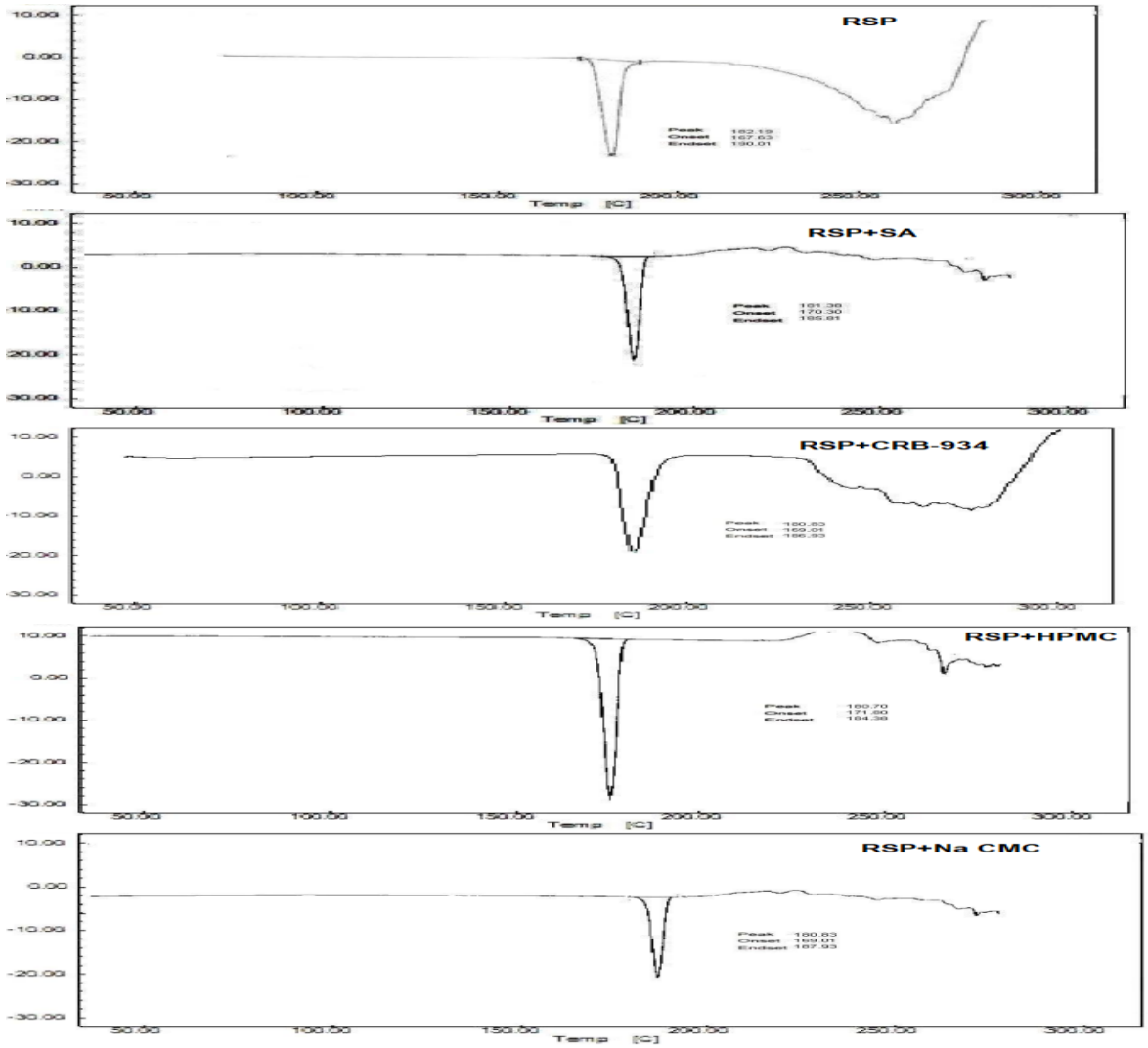


Figure. 5: DSC thermogram for Risperidone and Risperidone with Polymers

3.3 Evaluation of Risperidone Loaded Mucoadhesive Buccal Patches

3.3.1. Physical Parameters

a) Physical appearance and surface texture of patches: These parameters were checked simply with visual inspection of patches and by feel or touch. The observation reveals that the patches are having smooth surface and they are elegant in appearance.

b) Weight uniformity of patches: The weight of the patches was determined using digital balance and the average weight of all patches was given in Table 6. The drug loaded patches (29 mm) were tested for uniformity of weight. The patches were found uniform in weight. The average weight of eight formulations in the range of 25.00 ±1.73 to 47.66±0.57 mg respectively.

c) Thickness of patches: The thickness of the patches was measured using screw gauge and the average thickness of all patches was given inTable 6.The drug loaded patches (29 mm) were tested for thickness. The average thickness of eight formulations in the range of 0.52±0.01 mm to 0.58±0.05 mm respectively.

d) Folding endurance of patches: The folding endurance gives the idea of flexible nature of patches. The folding endurance was measured manually, patches were folded repeatedly till it broke, and it was considered as the end point. The folding endurance was found optimum and the patches exhibited good physical and mechanical properties and the average folding endurance of all patches in the range of 238±1.95 to 293.33±2.64 respectively was given in Table 6.

e) Surface pH of patches: Surface pH was determined by bring the patches in contact with 1ml of distilled water. The surface pH was noted by bringing a combined glass electrode or pH paper near the surface of patches and allowing equilibrate for 1 min and the average surface pH of all patches was given in Table 6.

f) Drug content uniformity of patches:

Risperidone buccal patches prepared with various polymers were subjected to the evaluation for uniform dispersion of drug throughout the patch. In each case three patches were used and the average drug content was calculated, the results were represented in Table-7. The drug was dispersed in the range of 90.14 ± 0.07 to 98.75 ± 0.80 %. Suggesting that drug was uniformly dispersed throughout all prepared patches.

3.3.2. Mechanical parameters

a) In-vitro residence time of patches

The in vitro residence time was determined by employing a modified USP disintegration apparatus. The average In-vitro residence time of all patches was given in Table 7. In vitro residence time for various patches prepared was in the range of 3.16±0.12 to 7.15±0.13 hours depending on the mucoadhesion properties of the polymer used. This increased residence time that was mainly due to the strong mucoadhesive property of the Carbopol.

b) In-vitro drug release profile from buccal patches

The data of *in- vitro* drug release profile from buccal patches varied with respect to the polymer composition and nature. An increase in drug release from the buccal patches was found with increasing concentration of polymers that were more hydrophilic in nature. Among all formulations, the formulation F6 was shown maximum in-vitro drug released (82.03 ±0.82 %) over a period of 7 hours was observed. All the in-vitro drug release profiles were represented in table 8.

c) Ex-vivo permeation from buccal patches

The Ex-vivo permeation from buccal patches varied with respect to the polymer composition and nature. An increase in drug release from the buccal patches was found with increasing concentration of polymers that were more hydrophilic in nature. Among all formulations, the formulation F6 was shown maximum Ex-vivo permeation (75.21 ± 0.42%) over a period of 7 hours were observed. All the data of diffusion profiles were represented in table 9.

Table. 6: Physical evaluation of mucoadhesive buccal patches of Risperidone

Formulations	Average Weight(mg)	Average Thickness(mm)	Average Folding Endurance	Surface pH
F1	34.66±1.15	0.55±0.05	263.33±3.51	6.33±0.05
F2	43.33±1.15	0.52±0.05	266.66±3.51	5.76±0.11
F3	33.33±1.15	0.58±0.01	243.33±2.08	6.46±0.05
F4	28.66±1.15	0.53±0.05	287.33±4.50	6.43±0.35
F5	25.000±1.73	0.57±0.05	249.66±2.08	5.8±0.37
F6	27.66±1.52	0.52±0.01	293.33±2.64	6.4±0.26
F7	45.66±1.52	0.54±0.05	238±1.95	5.76±0.15
F8	47.66±0.57	0.58±0.05	276.66±2.0	6.33±0.20

*All values are expressed as mean± S.D., n=3

Table. 7: Data of in vitro residence time and drug content uniformity

Formulations	In Vitro Residence time (Hours)	Drug Content Uniformity %
F1	3.43±0.12	93.38±0.27
F2	3.49±0.09	92.36±0.11
F3	4.24±0.13	94.01±0.40
F4	4.11±0.05	91.27±0.49
F5	6.47±0.15	96.79±0.07
F6	7.15±0.13	98.75±0.80
F7	5.24±0.11	92.95±0.11
F8	5.34±0.12	96.88±0.81

*All values are expressed as mean± S.D., n=3

Table. 8: Data of *in-vitro* release profile of Risperidone loaded mucoadhesive buccal patches

Time (Hrs)	F1	F2	F3	F4	F5	F6	F7	F8
1	22.18±1.12	22.18±0.49	22.81±1.52	23.75±0.94	26.71±1.82	25.15±1.12	21.71±0.18	23.43±0.56
2	27.34±0.12	29.18±0.15	28.90±0.62	30.93±0.67	34.68±1.12	36.71±1.22	29.37±0.19	28.9±1.12
3	35.15±0.42	34.06±1.02	37.18±0.42	38.59±1.32	41.71±0.52	44.53±1.22	37.65±0.60	35.93±1.22
4	42.03±0.32	40.78±0.54	43.28±1.72	44.37±1.42	49.84±0.90	50.78±0.42	44.53±1.52	42.3±0.14
5	53.43±1.12	49.78±0.70	51.56±1.12	53.43±1.10	56.71±1.14	57.96±0.62	53.25±0.56	49.53±0.22
6	61.71±1.42	57.96±0.50	64.37±0.10	66.09±0.70	68.43±0.82	69.53±0.70	60.46±0.19	58.12±1.32
7	67.34±0.52	64.84±1.14	67.34±0.68	68.75±0.92	73.59±0.72	74.21±1.12	70.62±0.16	65.15±1.42
8	72.34±0.92	68.15±1.18	70.15±0.82	71.87±0.14	75.46±0.23	78.43±0.42	75.93±0.72	72.03±0.98
9	74.27±1.16	70.78±1.02	71.10±1.52	73.43±0.13	77.50±1.22	82.03±0.82	78.28±1.22	75.78±0.18

*All values are expressed as mean± S.D., n=3

Table 9: Data of Ex-vivo permeation release studies of Risperidone loaded mucoadhesive buccal patches

Time (Hrs)	F1	F2	F3	F4	F5	F6	F7	F8
1	17.68±1.12	16.20±0.72	16.20±0.82	18.01±0.18	18.50±1.12	20.30±1.82	18.01±0.87	18.50±1.02
2	22.05±0.15	21.93±0.16	21.93±0.10	24.70±0.67	26.87±0.10	25.70±0.10	23.55±1.12	24.90±0.57
3	28.78±0.60	28.83±0.10	27.85±0.17	30.99±0.34	32.68±0.19	34.36±0.12	31.06±0.02	29.07±0.62
4	36.26±1.72	34.51±1.52	35.91±0.82	38.13±0.12	40.26±1.62	41.58±1.10	38.05±0.92	36.54±1.12
5	42.36±1.10	39.99±0.40	41.83±1.12	42.87±1.12	43.50±0.92	48.52±0.19	43.12±0.12	41.50±1.72
6	48.91±0.19	46.86±1.32	46.06±0.10	47.62±1.22	49.32±0.10	59.24±0.49	48.88±0.87	46.97±0.56
7	59.05±0.13	57.03±1.12	56.48±0.85	58.10±0.14	61.32±0.12	65.32±0.95	55.69±1.10	54.31±1.19
8	64.99±1.12	63.51±1.19	62.74±1.02	66.40±0.18	68.18±0.14	70.92±1.92	62.32±1.02	61.02±0.92
9	66.10±0.60	64.88±1.15	64.23±1.02	68.12±0.45	71.64±0.92	75.21±0.42	68.71±1.42	66.53±0.12

*All values are expressed as mean± S.D., n=3

d). Design of an Experiment

In-vitro release profile

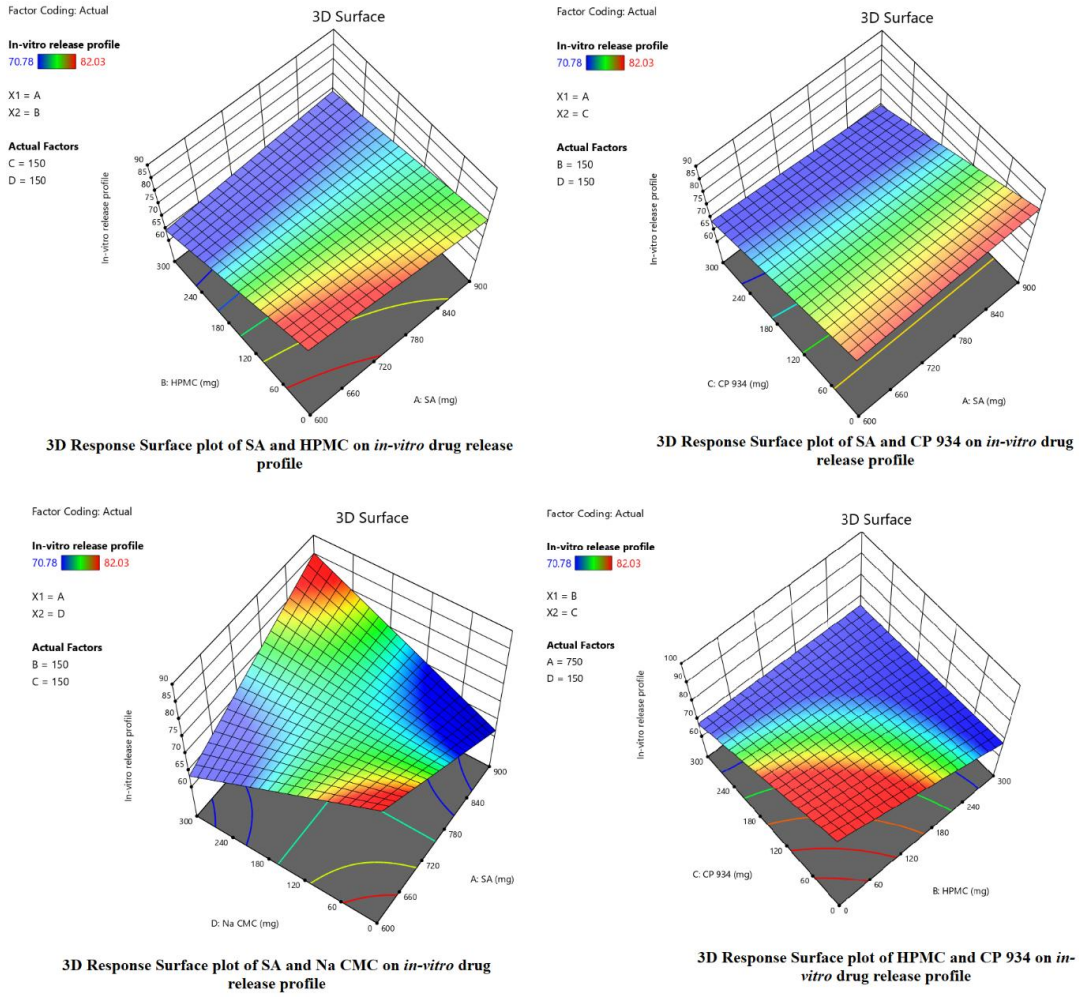
The changes in the proportions of X1, X2, and X3 caused a variation in dependent variables. The release characteristics of Formulation F6, which contained 600 mg SA, 100 mg of HPMC and 300 mg of CP 934, were satisfactory (82.03 ±0.82 %) over a period of 7 hours showing to variations in the natural polymer concentration represented in figure 6.

In-vitro release profile =74.4575 + -0.825 * A + -7.5 * B + -7.695 * C + 3.3675 * AB + -1.1925 * AC + 11.8162 * AD + 6.56625 * BC

Ex-vivo permeation release

The changes in the proportions of X1, X2, and X3 caused a variation in dependent variables. The Ex-vivo permeation release characteristics of Formulation F6, which contained 600 mg SA, 100 mg of HPMC and 300 mg of CP 934, were satisfactory (75.21±0.42) over a period of 7 hours showing to variations in the natural polymer concentration represented in figure 7.

Ex-vivo permeation release = 71.1529 + 1.71125 * A + -0.35125 * B + 0.1625 * C + 3.93375 * AB + 0.615 * AC + 6.9225 * AD + 6.39 * BC



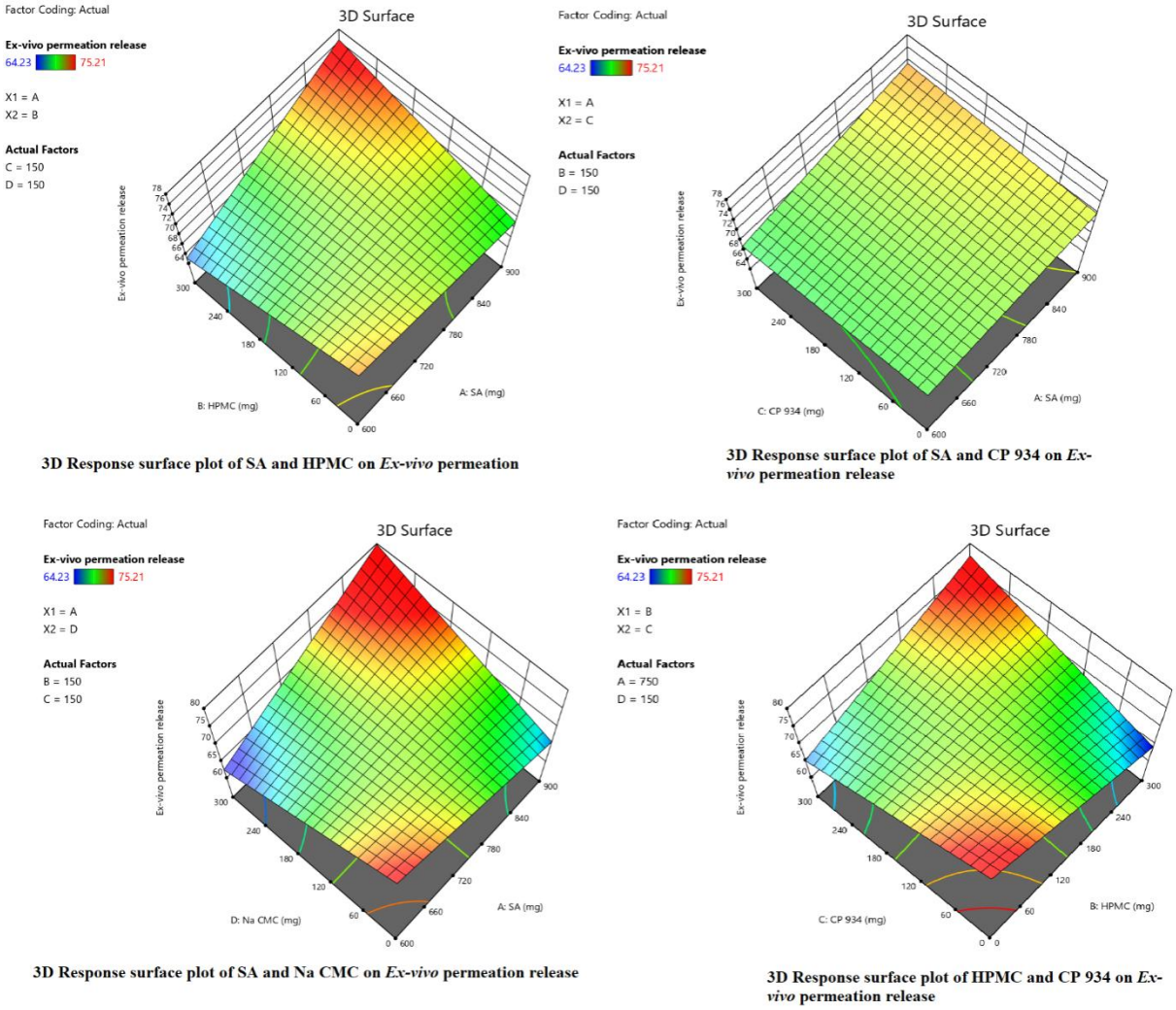
3D Response Surface plot of SA and HPMC on *in-vitro* drug release profile

3D Response Surface plot of SA and CP 934 on *in-vitro* drug release profile

3D Response Surface plot of SA and Na CMC on *in-vitro* drug release profile

3D Response Surface plot of HPMC and CP 934 on *in-vitro* drug release profile

Figure 6: 3D Response Surface plot of polymer combination on *in-vitro* drug release profile



3D Response surface plot of SA and HPMC on *Ex-vivo* permeation

3D Response surface plot of SA and CP 934 on *Ex-vivo* permeation release

3D Response surface plot of SA and Na CMC on *Ex-vivo* permeation release

3D Response surface plot of HPMC and CP 934 on *Ex-vivo* permeation release

Figure 7: 3D Response Surface plot of polymer combination on *Ex-vivo* permeation release

e) Stability Studies

The formulation F6 was further subjected to stability study at specified period in appropriate storage condition as per ICH guidelines. The formulation was monitored for appearance, surface pH, drug content, *In-Vitro* residence time, *In-Vitro* drug released and *Ex-Vivo* permeation and results were represented in Table 10.

Table10: Data of stability studies of formulation F6

Stability studies	Appearance	Surface pH	Content uniformity (%)	In-vitro residence time (hr)	In-vitro drug release	Ex-vivo Permeation
Initial	6.40±0.26	98.75±0.80	7.15±0.13	82.03±0.82	75.21±0.42	6.40±0.26
First month	6.29±0.09	98.22±0.20	7.05±0.05	81.86±0.07	75.03±0.05	6.29±0.09
Second month	6.20±0.01	98.18±0.03	6.45±0.05	81.52±0.08	74.52±0.12	6.20±0.01
Third month	6.09±0.03	98.05±0.04	6.27±0.02	80.33±0.06	74.09±0.73	6.09±0.03

4. Conclusion

FTIR and DSC investigations indicated that Risperidone was completely entrapped in the polymer carrier bonds and had no chemical interaction. Smooth, attractive patches were made. Patches made with varying polymer concentrations weighed 25 ±1.73 to 47.66 ±0.57 mg. Patch folding endurance ranged from 238.0 ±1.95 to 293.33 ±2.64. Formulation F6 patches had high swelling index values of 25.01% after 7hr owing to carbopol 934's excessive swelling. All patches had surface pH between 5.76±0.11 and 6.46±0.05pH. Depending on polymer mucoadhesion, patches had an in vitro residence duration of 3.16±0.12 to 7.15±0.13 hours. Due to Carbopol's mucoadhesiveness, residence duration increased. The buccal patches' drug content uniformity was assessed at 90.14± 0.07 and 98.75± 0.80 %, indicating uniform distribution. Polymer composition and type affected buccal patch medication release and penetration. Hydrophilic polymers increased buccal patch medication release. F6 was the finest of the F1–F8 formulas. Formulation F6 in-vitro drug release was 82.03 ±0.82% and ex-vivo permeability was 75.21 ± 0.42% after 7 hours. • Stability studies showed no significant change in appearance, surface pH, content homogeneity, in-vitro residence duration, drug release, or ex-vivo penetration. F6 was steady. • Risperidone (50 mg), sodium alginate (600 mg), HPMC (100 mg), and carbopol 934 (300 mg) in formulation F6 had an acceptable release profile. The optimum formulation is F6.

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Disclosure

The author reports no conflicts of interest in this work and is responsible for the content and writing of this paper.

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