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# FORMULATION AND EVALUATION OF BUCCAL PATCH OF PAROXETINE HYDROCHLORIDE

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**Abstract:** Present work was under taken for development of buccal patch of Paroxetine HCl to overcome the limitations of current routes of administration. Buccal patch was developed to bypass the hepatic metabolism with possible increase in the bioavailability. Controlled drug delivery from patch can reduce undesirable fluctuation of drug levels enhancing therapeutic effect and eliminating side effect. Buccal patches were prepared by using combination of bioadhesive polymers and a release control polymers. Optimization of formulation was carried out using $3^2$ full factorial experimental design, where in the ratio of polymer (Xanthan gum: PVA) and type of plasticizer were chosen as independent variables, while tensile strength, *ex vivo* mucoadhesive strength and similarity factor ($f_2$) were selected as dependent variables. The prepared patches were evaluated for thickness, folding endurance, tensile strength, *ex vivo* mucoadhesive strength, swelling study, *in vitro* drug release and *ex vivo* permeation study. The optimized formulation (batch F7) containing Xanthan gum and PVA showed greater similarity factor with theoretical drug release profile of drug ($f_2$=66.79), satisfactory *ex vivo* permeation study (90.45%) and physicomechanical properties that were suitable for buccal patch. Optimized formulation exhibited stability at accelerated environmental conditions for 1 month.

**Keywords:** Buccal Patch, Paroxetine HCl, Xanthan gum, $3^2$ full factorial design

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## INTRODUCTION

Amongst the various routes of drug delivery, oral route is perhaps the most preferred by the patients and the clinicians. However, per oral administration of drugs has disadvantages such as hepatic first pass metabolism and enzymatic degradation within the GI tract, that prohibit oral administration of certain classes of drugs especially peptides and proteins. Consequently, other absorptive mucosae are considered as potential sites for drug administration.

Buccal route of drug delivery provides the direct access to the systemic circulation through the jugular vein bypassing the first pass hepatic metabolism leading to high bioavailability. Other advantages such as excellent accessibility, low enzymatic activity, suitability for drugs or excipients that mildly and reversibly damage or irritate the mucosa, painless administration, easy withdrawal, facility to include permeation enhancer/ enzyme inhibitor or pH modifier in the formulation, versatility in designing as multidirectional or unidirectional release system for local or systemic action.[1-5]

Paroxetine HCl is a second generation antidepressant more potent than other drugs. It shows extensive first pass metabolism when given by gastrointestinal (GI) route.[6] Hence, present work was under taken for development of buccal patch of Paroxetine HCl to overcome the limitations of current routes of administration bypassing the hepatic metabolism with possible increase in the bioavailability.

## MATERIALS AND METHODS

Paroxetine HCl was gifted Zydus Cadila Healthcare Ltd., Ahmedabad, India. Xanthan gum was procured from Yarrow Chem, Mumbai, India. PVA was supplied by Chemdyes Corporation, Ahmedabad, India. Propylene glycol was supplied by Finar Chemicals Ltd., Ahmedabad, India. All the materials used were of pharmaceutical or analytical grade.

### Preparation of Buccal Patch

Bioadhesive polymer and release controlled polymer were dissolved in water (7 ml). After that in the other beaker drug was dissolved in ethanol (3 ml). Both the solutions were mixed and then plasticizer (40%) was added into the solution with constant stirring. Solvent casting technique was used for preparation of patches. The solution was casted into petridish and was covered with inverted funnel for the controlled evaporation of the solvent. These were kept in hot air oven (60-80 $^0$C) for the 4-5 h, till the flexible patch was formed with complete removal of solvent.

**Preliminary Screening of Bioadhesive Polymer**

Bioadhesive polymer is necessary for adhesion of buccal patch to buccal mucosa. It is necessary to select good bioadhesive polymer for adherence of buccal patch to mucosa for at least 8 h of time. For optimization of bioadhesive polymer, five different bioadhesive polymers were taken. Compositions of formulation for screening of bioadhesive polymer are shown in Table 1. Formulations were evaluated for *ex vivo* mucoadhesive strength, tensile strength, thickness and folding endurance.

**Table 1: Compositions of formulation for selection of bioadhesive polymer**

| Ingredients | Quantity in mg | | | | |
|---|---|---|---|---|---|
| | **OP1** | **OP2** | **OP3** | **OP4** | **OP5** |
| **Paroxetine HCl** | 240 | 240 | 240 | 240 | 240 |
| **Sodium alginate** | 500 | | | | |
| **Sodium CMC** | | 500 | | | |
| **Gelatin** | | | 500 | | |
| **Xanthan gum** | | | | 500 | |
| **Carbopol 934P** | | | | | 500 |
| **PG (40%)** | 200 | 200 | 200 | 200 | 200 |
| **DW + Ethanol (7:3) (ml)** | 10 | 10 | 10 | 10 | 10 |

**CMC: Carboxy methyl cellulose; PG: Propylene glycol; DW: Distilled water**

**Preliminary Screening of Release Controlled Polymer [7]**

Controlled release polymer is necessary for controlled the drug release for prolonged time. For optimization of controlled release polymer, different concentration and different grade of HPMC, PVP K-30 and PVA were selected. Compositions of formulation for optimization are shown in Table 2. Formulations were evaluated for *in vitro* drug release for optimization.

**Table 2: Compositions of formulation for optimization of controlled release polymer**

| Ingredients | Quantity in mg | | | | |
|---|---|---|---|---|---|
| | **P1** | **P2** | **P3** | **P4** | **P5** |
| **Paroxetine HCl** | 240 | 240 | 240 | 240 | 240 |
| **Xanthan gum** | 300 | 300 | 300 | 300 | 300 |
| **PVA (Poly Vinyl Alcohol)** | 200 | | | | |
| **PVP K-30** | | 200 | | | |
| **HPMC K4M** | | | 200 | | |
| **HPMC K15M** | | | | 200 | |
| **HPMC E15** | | | | | 200 |
| **PG (40%)** | 200 | 200 | 200 | 200 | 200 |
| **DW + Ethanol (7:3) (ml)** | 10 | 10 | 10 | 10 | 10 |

**PVP: Poly Vinyl Pyrolidone; HPMC: Hydroxy Propyl Methyl Cellulose; PG: Propylene Glycol; DW: Distilled Water**

**Drug-Excipients Compatibility Study**

Fourier transform infrared (FTIR) technique was used to study the physical and chemical interaction between drug and excipients used. FTIR spectra of pure drug and drug with the excipients were recorded using KBr mixing method on FTIR instrument available at central instrument laboratory of the institute (FTIR-1700, Shimadzu, Kyoto, Japan).

**Full Factorial Design**

**Optimization by $3^2$ full factorial design**

A $3^2$ randomized full factorial design was used in the present investigation. In this design two factors are evaluated, each at 3 levels, and experimental trials are performed at all 9 possible combinations. The ratio of polymer (Xanthan gum: PVA) and type of plasticizer were chosen as independent variables in $3^2$ full factorial design, , while dependent variables selected were

tensile strength, *ex vivo* mucoadhesive strength and similarity factor ($f_2$). The coding of variables and formulation layout for factorial batches are shown in Table 3 and 4, respectively.

**Table 3: Coding of variables**

| Level | Factor X1<br>Ratio of polymer<br>(Xanthan gum : PVA) | Factor X2<br>Type of plasticizer |
|---|---|---|
| **-1** | 40:60 | Propylene glycol |
| **0** | 50:50 | Glycerine |
| **+1** | 60:40 | PEG 400 |

**Table 4: Formulation layout of factorial batches**

| Batch | Factor X1 | Factor X2 |
|---|---|---|
| **F1** | -1 | -1 |
| **F2** | -1 | 0 |
| **F3** | -1 | +1 |
| **F4** | 0 | -1 |
| **F5** | 0 | 0 |
| **F6** | 0 | +1 |
| **F7** | +1 | -1 |
| **F8** | +1 | 0 |
| **F9** | +1 | +1 |

**Preparation of the Backing layer for the Optimized batch**

**Table 5: composition for the backing layer**

| Ingredients | Quantity in mg |
|---|---|
| **Ethyl Cellulose** | 750 |
| **PG (40%)** | 300 (0.28 ml) |
| **Ethanol (ml)** | 10 |

**RESULTS AND DISCUSSION**

**Selection of Bioadhesive Polymer**

**Table 6: Selection of bioadhesive polymer**

| Batch | Thickness(mm) | Folding endurance | Tensile strength (g/mm) | Ex vivo mucoadhesion strength (g force) |
|---|---|---|---|---|
| **OP1** | 0.23±0.005 | >200 | 2.0±0.2 | 10.35±0.04 |
| **OP2** | 0.15±0.01 | >200 | 0.5±0.05 | 5.93±0.02 |
| **OP3** | 0.13±0.01 | >200 | 2.0±0.1 | 7.33±0.3 |
| **OP4** | 0.25±0.03 | >200 | 2.5±0.2 | 13.2±0.2 |
| **OP5** | Not separated from Petri plate | | | |

Among all the batches, batch OP4 containing xanthan gum given more mucoadhesive strength. So it was selected for further batches.

**Selection of Release Controlled Polymer**

**Table 7: Screening of release controlled polymer**

| Time (hr) | Cumulative Percentage Release (%CPR) | | | | |
|---|---|---|---|---|---|
| | **P1** | **P2** | **P3** | **P4** | **P5** |
| **1** | 24.08 | 19.90 | 17.04 | 11.28 | 22.2 |
| **2** | 33.11 | 28.99 | 18.70 | 15.64 | 28.28 |
| **3** | 39.24 | 32.34 | 29.28 | 18.28 | 33.64 |
| **4** | 51.11 | 42.73 | 40.71 | 20.07 | 37.42 |
| **5** | 62.94 | 52.76 | 52.99 | 22.02 | 45.49 |
| **6** | 74.01 | 63.37 | 61.43 | 25.51 | 58.06 |
| **7** | 85.40 | 74.04 | 74.09 | 32.45 | 67.42 |
| **8** | 98.44 | 87.72 | 83.51 | 41.37 | 82.37 |

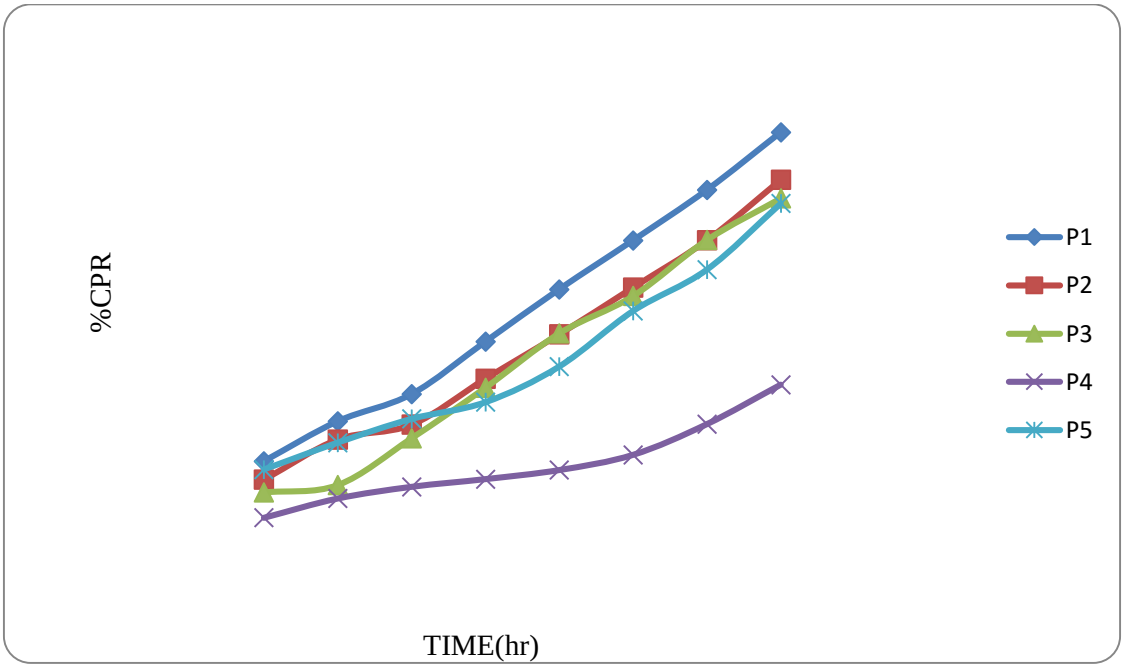


**Figure 1: Comparison of release pattern**

**Table 8: Selection of release controlled polymer**

| Batch | Thickness(mm) | Folding endurance | Tensile strength(g/mm) | %CPR |
|---|---|---|---|---|
| **P1** | 0.31±0.005 | >300 | 2.0±0.1 | 98.44 |
| **P2** | 0.27±0.01 | >300 | 0.5±0.15 | 87.72 |
| **P3** | 0.21±0.02 | >300 | 1.8±0.2 | 83.51 |
| **P4** | 0.28±0.01 | >300 | 0.75±0.02 | 41.37 |
| **P5** | 0.20±0.03 | 144 | 1.8±0.05 | 82.37 |

Among all five batches P1 Batch containing xanthan gum and PVA showed 98.44% drug released in 8 h (Figure 1). Hence it was selected for further study.

**Drug Excipient Compatibility Study**

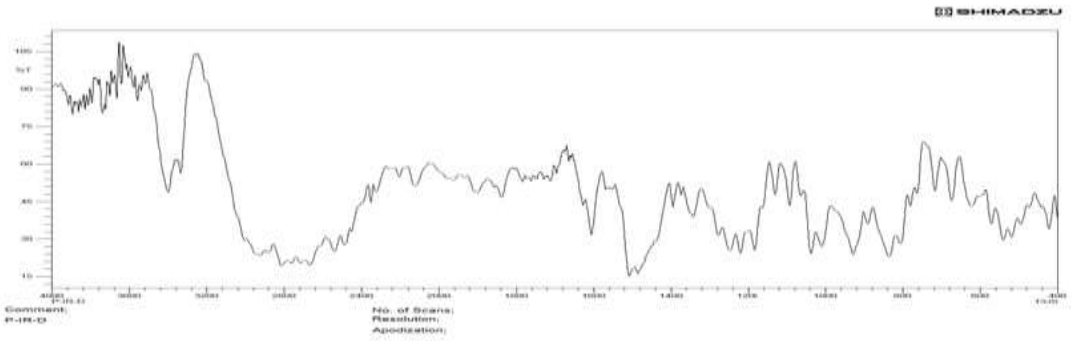

**Figure 2: FTIR Spectra of Paroxetine HCl**

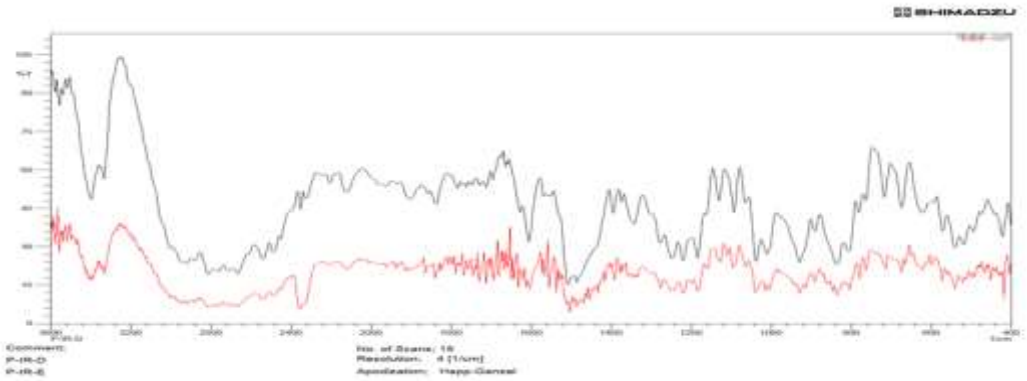

**Figure 3: FTIR overlay spectra of drug and mixture**

The frequencies of functional groups of the drug Paroxetine HCl remained intact in physical mixture containing different excipients (Figure 2 and 3). So, it was concluded that there was no major interaction occurred between the drug and excipients used in the study.

**Optimization of Factorial Batches**

**Table 9: Physicomechanical properties of buccal patch of Paroxetine HCl**

| Batch Code | Thickness (mm) | Folding Endurance | Surface pH | Drug Content | Tensile Strength (g/mm) |
|---|---|---|---|---|---|
| **F1** | 0.23±0.015 | 246 | 6.32±0.015 | 99.10±0.36 | 0.8±0.1 |
| **F2** | 0.24±0.015 | >300 | 6.44±0.017 | 98.87±0.90 | 1.13±0.20 |
| **F3** | 0.25±0.020 | 274 | 6.58±0.015 | 97.93±0.45 | 1.3±0.2 |
| **F4** | 0.24±0.02 | >300 | 6.26±0.030 | 99.10±0.96 | 1.53±0.15 |
| **F5** | 0.26±0.015 | >300 | 6.70±0.015 | 97.03±1.05 | 1.96±0.15 |
| **F6** | 0.27±0.026 | >300 | 6.47±0.015 | 99.47±0.93 | 1.3±0.2 |
| **F7** | 0.26±0.025 | >300 | 6.98±0.005 | 100.03±0.12 | 2.0±0.3 |
| **F8** | 0.24±0.015 | >300 | 7.01±0.035 | 98.16±0.35 | 1.83±0.25 |
| **F9** | 0.25±0.02 | >300 | 6.33±0.005 | 99.60±0.51 | 1.3±0.2 |

**Table 10: Swelling index of factorial batches**

| Batch | Swelling Index | | |
|---|---|---|---|
| | **At 1 hr** | **At 4 hr** | **At 8 hr** |
| **F1** | 47.22 | 72.52 | 76.57 |
| **F2** | 54.77 | 67.56 | 75.56 |
| **F3** | 59.78 | 71.13 | 83.71 |
| **F4** | 75.87 | 80.36 | 86.33 |
| **F5** | 38.12 | 83.13 | 86.42 |
| **F6** | 62.06 | 77.03 | 95.02 |
| **F7** | 63.44 | 88.51 | 102.86 |
| **F8** | 63.55 | 104.87 | 114.05 |
| **F9** | 52.76 | 79.56 | 97.38 |

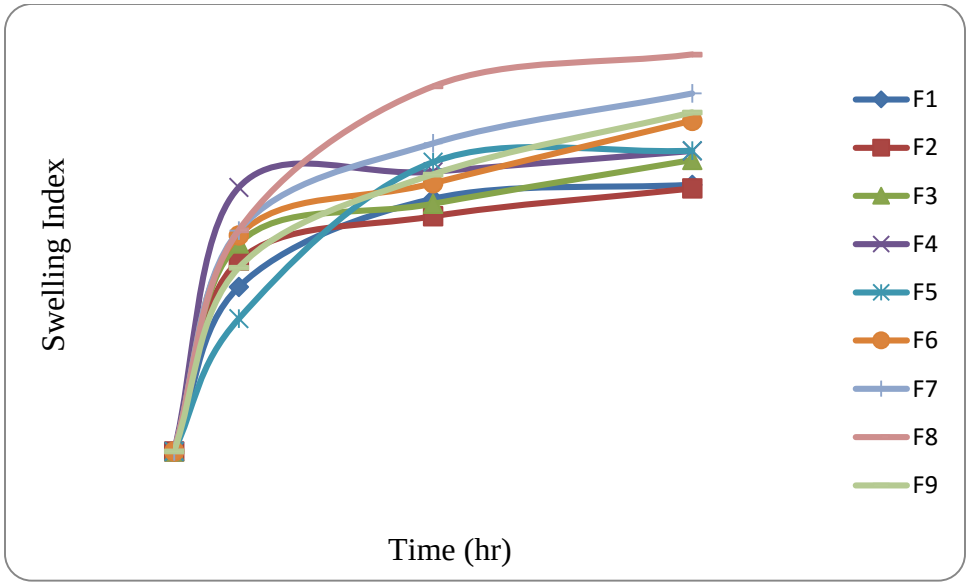


**Figure 4: plot of swelling index vs. time**

**Table 11: In vitro mucoadhesive study of buccal patch of Paroxetine HCl**

| Batch | *Ex vivo mucoadhesive strength (g force) | *Ex vivo mucoadhesion time (hr) |
|---|---|---|
| **F1** | 10.90±0.33 | 5.68±1.15 |
| **F2** | 11.86±0.36 | 6.47±0.58 |
| **F3** | 11.78±0.55 | 6.98±1.23 |
| **F4** | 11.88±0.45 | 8.67±0.58 |
| **F5** | 13.11±0.99 | 7.69±0.86 |
| **F6** | 13.14±0.23 | 6.33±1.00 |
| **F7** | 13.19±0.86 | 9.67±0.58 |
| **F8** | 13.28±0.72 | 10.52±1.15 |
| **F9** | 13.80±0.41 | 9.27±0.53 |

***values are mean ± standard deviation for 3 determinations.**

**Table 12: In vitro dissolution profiles of factorial batches**

| Time (hr) | % CPR | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** | **F7** | **F8** | **F9** |
| **1** | 18.12±0.30 | 24.31±0.38 | 21.31±0.43 | 24.08±0.27 | 18.61±0.37 | 23.91±0.27 | 19.18±0.48 | 19.26±0.37 | 18.74±0.54 |
| **2** | 27.83±0.74 | 37.18±0.19 | 36.18±0.37 | 32.15±0.29 | 38.14±0.43 | 32.86±0.34 | 27.33±0.51 | 27.35±0.55 | 27.11±0.14 |
| **3** | 42.80±0.84 | 49.82±0.57 | 51.82±0.28 | 41.24±0.46 | 51.47±0.48 | 41.23±0.84 | 42.47±0.46 | 41.09±0.36 | 41.13±0.82 |
| **4** | 59.44±0.41 | 63.23±0.27 | 62.14±0.42 | 58.77±0.49 | 61.78±0.27 | 53.13±0.64 | 57.25±0.42 | 58.16±0.34 | 58.98±0.43 |
| **5** | 73.48±1.16 | 78.67±0.36 | 72.61±0.41 | 67.54±0.16 | 70.35±0.89 | 63.29±0.32 | 67.29±0.40 | 68.07±0.53 | 68.85±0.29 |
| **6** | 89.24±0.64 | 88.99±0.35 | 82.43±0.48 | 78.01±0.54 | 81.25±0.42 | 74.13±0.37 | 78.36±0.54 | 78.14±0.22 | 79.35±0.45 |
| **7** | 99.29±0.98 | 99.95±0.31 | 89.45±0.54 | 85.40±0.41 | 90.21±0.35 | 85.43±0.52 | 86.71±0.47 | 86.66±0.48 | 87.23±0.28 |
| **8** | | | 96.12±0.70 | 96.44±0.46 | 98.35±0.47 | 96.07±0.58 | 99.65±0.42 | 98.71±0.48 | 98.85±0.39 |

***values are mean ± standard deviation for 3 determinations.**

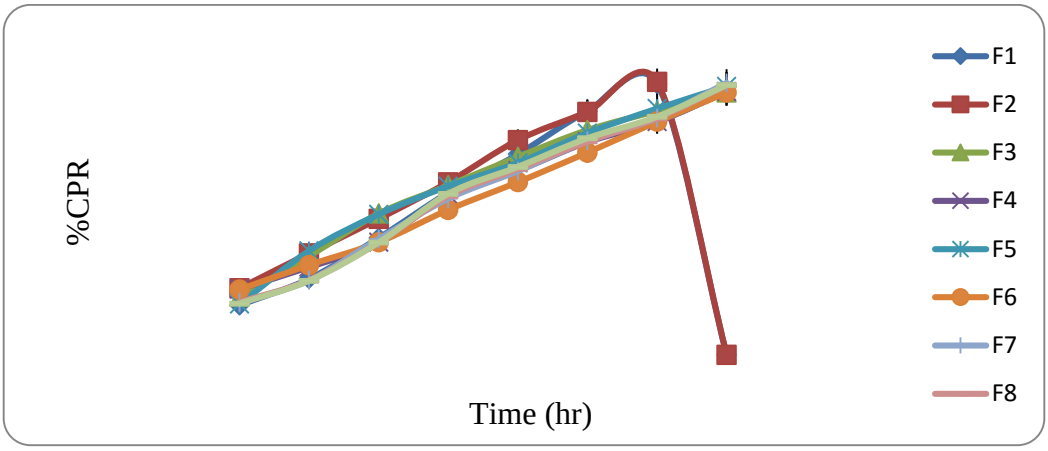


**Figure 5: Plot of %CPR Vs Time for all batches**

**Table 13: Similarity factor (f2) of buccal patch of Paroxetine HCl [8]**

| Batch code | Similarity Factor ($f_2$) |
|---|---|
| **F1** | 21.91 |
| **F2** | 21.31 |
| **F3** | 51.03 |
| **F4** | 59.42 |
| **F5** | 52.04 |
| **F6** | 62.85 |
| **F7** | 66.79 |
| **F8** | 66.07 |
| **F9** | 64.73 |

Batch F7 showed maximum similarity ($f_2$ = 66.79) compared with other batches.

**Factorial Design Data Analysis**

The data of factorial design batches were analyzed using Design Expert Software 9.0.4 version. The full and reduced models were developed using the co-efficients for all the selected dependent variables.

***Full and Reduced Model for Tensile Strength ($Y_1$)***

The summary of regression analysis for tensile strength is shown in Table 14 along with the equations for full and reduced models. In developing the reduced model, the co-efficients with insignificance ($p > 0.05$) were removed. From the result of regression statistics it was concluded that ratio of polymers had significant contribution in prediction of tensile strength while interaction between X1 and X2 was insignificant. The data are also represented by 3D response surface plot as shown in Figure 6.

**Table 14: Summary output of regression analysis for effect of $X_1$ and $X_2$ on $Y_1$**

**REGRESSION STATISTICS**

| | | | | | |
|---|---|---|---|---|---|
| **R Square** | | | 0.9634 | | |
| **Adjusted R Square** | | | 0.9025 | | |
| **Adeq. Precision** | | | 11.920 | | |
| **Model** | | | Quadratic | | |
| **Observations** | | | 9 | | |
| | **DF** | **SS** | **MS** | **F** | **P- value** |
| **Regression** | 5 | 1.26 | 0.25 | 15.81 | 0.0230 |
| **Residual** | 3 | 0.04 | 0.016 | | |
| **Total** | 8 | 1.31 | | | **Significant** |

**Full Model**

**$Y_1 = 1.86 + 0.31 X_1 - 0.005 X_2 - 0.3 X_1^2 - 0.33 X_2^2 - 0.20 X_1 X_2$**

**Reduced Model**

**$Y1 = 1.86 + 0.31 X_1 - 0.3 X_1^2 - 0.33 X_2^2$**

***Full and Reduced Model for Ex Vivo Mucoadhesion Strength ($Y_2$)***

The summary of regression analysis for *ex vivo* mucoadhesive strength is shown in Table 15 along with the equations for full and reduced models. In developing the reduced model, the co-

efficients with insignificance ($p > 0.05$) were removed. From the result of regression statistics it was concluded that ratio of polymers and type of plasticizers had significant contribution of *ex vivo* mucoadhesive strength while interaction between X1 and X2 was insignificant. The data are also represented by 3D response surface plot as shown in Figure 7.

**Table 15: Summary output of regression analysis for effect of $X_1$ and $X_2$ on $Y_2$**

**REGRESSION STATISTICS**

| | | | | | |
|---|---|---|---|---|---|
| **R Square** | | | 0.9517 | | |
| **Adjusted R Square** | | | 0.8713 | | |
| **Adeq. Precision** | | | 10.029 | | |
| **Model** | | | Quadratic | | |
| **Observations** | | | 9 | | |
| | **DF** | **SS** | **MS** | **F** | **P- value** |
| **Regression** | 5 | 7.04 | 1.40 | 11.83 | 0.0344 |
| **Residual** | 3 | 0.35 | 0.11 | | |
| **Total** | 8 | 7.40 | | | **Significant** |

**Full Model**

$$Y_2 = 12.91 + 0.95\,X_1 + 0.45\,X_2 - 0.06\,X_1^2 - 0.24\,X_2^2 - 0.30\,X_1X_2$$

**Reduced Model**

$$Y_2 = 12.91 + 0.95\,X_1 + 0.45\,X_2$$

***Full and Reduced Model for Similarity Factor ($Y_3$)***

The summary of regression analysis for similarity factor is shown in Table 15 along with the equations for full and reduced models. In developing the reduced model, the co-efficients with insignificance ($p > 0.05$) were removed. From the result of regression statistics it was concluded that ratio of polymers had significant contribution in prediction of similarity factor while interaction between X1 and X2 was insignificant. The data are also represented by 3D response surface plot as shown in Figure 8.

**Table 16: Summary output of regression analysis for effect of $X_1$ and $X_2$ on $Y_3$**

**REGRESSION STATISTICS**

| | | | | | |
|---|---|---|---|---|---|
| **R Square** | | | 0.9558 | | |
| **Adjusted R Square** | | | 0.8820 | | |
| **Adeq. Precision** | | | 9.897 | | |
| **Model** | | | Quadratic | | |
| **Observations** | | | 9 | | |
| | **DF** | **SS** | **MS** | **F** | **P- value** |
| **Regression** | 5 | 2501.61 | 500.32 | 13.50 | 0.0304 |
| **Residual** | 3 | 111.14 | 37.04 | | |
| **Total** | 8 | 2612.75 | | | **Significant** |

**Full Model**

$$Y_3 = 52.73 + 17.29 X_1 + 5.00 X_2 - 7.90 X_1^2 - 9.39 X_2^2 + 8.05 X_1 X_2$$

**Reduced Model**

$$Y_3 = 52.73 + 17.29 X_1$$

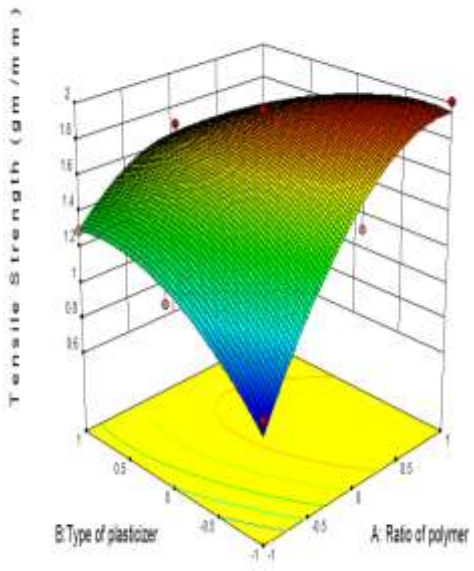


Figure 6:3D Surface plot of Response 1

(Tensile strength in g/mm)

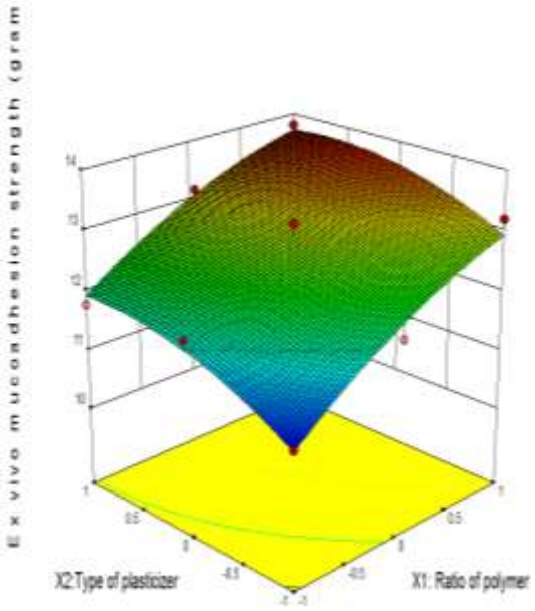


Figure 7: 3D Surface plot of Response 2

(Ex vivo mucoadhesive strength in gram force)

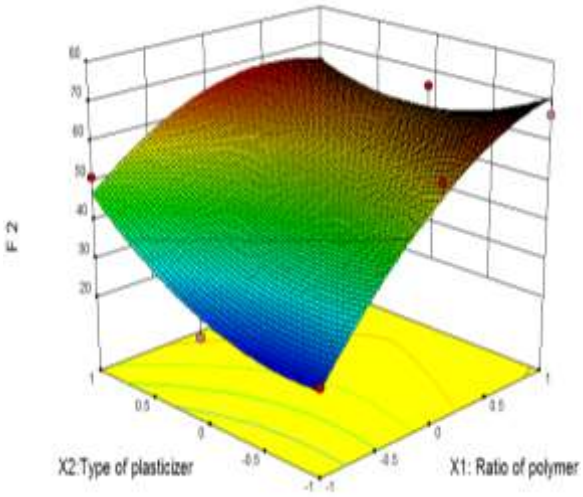


Figure 8: 3D Surface plot of Similarity factor

**Selection of Optimized Batch**

From the overlay plot it was seen that batch F4, F5, F6, F7 fall under the optimized area. In which the F7 batch having higher tensile strength, ex vivo mucoadhesion streangth as well as maximum similarity factor (66.79). So, F7 batch was the optimized batch.

***Ex Vivo* Permeation Study of Optimized Batch**

The study for *ex vivo* buccal permeation of drug was carried out for optimized batch of full factorial design. The permeation study of Paroxetine HCl through the goat buccal mucosa was performed using Franz diffusion cell at 37 ± 0.5 $^0$C. Fresh goat buccal mucosa was mounted between the donor and receptor compartments. The buccal patch was placed on the mucosa, and the compartments were clamped together. The donor compartment was filled with 1 ml of SSF. The receptor compartment (45 ml capacity) was filled with SSF and the hydrodynamics in the compartment was maintained by stirring with a magnetic bead at uniform slow speed. Five mL samples were withdrawn at predetermined time intervals and analyzed for drug content by UV spectrophotometer at 293 nm. The data are shown in Table 17. The correlation between % CPR and % CPP was determined as shown in Figure 9. The correlation between *in vitro* drug release and *ex vivo* permeation was found to be positive, with a correlation co efficient ($R^2$) of 0.995.

**Table 17: Ex vivo permeation study of optimized batch**

| Time (h) | %CPP |
|---|---|
| **1** | 17.35 |
| **2** | 25.42 |
| **3** | 37.85 |
| **4** | 52.64 |
| **5** | 64.86 |
| **6** | 73.19 |
| **7** | 83.46 |
| **8** | 90.45 |

**% CPP is Cumulative Percentage of drug Permeated**

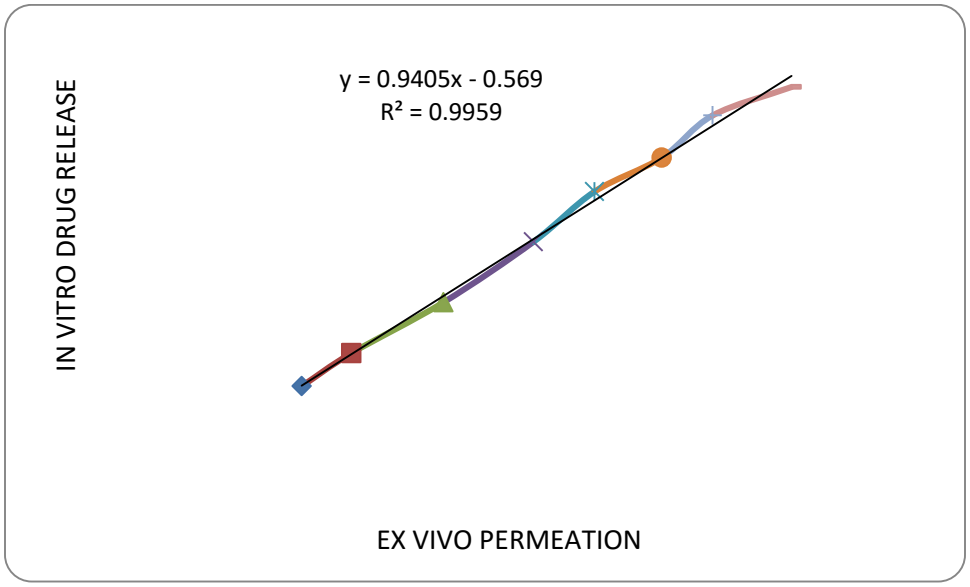


**Figure 9: Correlation between *in vitro* drug release and *ex vivo* drug permeation**

**Kinetic Modeling of Dissolution Data**

The dissolution data were fitted to various models like zero order, Higuchi model [9], Hixon Crowell model [10] and Korsemeyer-Peppas model[11]. The data were fitted to zero order model with correlation co-efficient of 0.997. In case of the controlled or sustained release formulations, diffusion, swelling and erosion are the three most important rate controlling mechanisms. Formulation containing swelling polymers show swelling as well as diffusion mechanism because the kinetic of swelling include relaxation of polymer chains and imbibitions of water, causing the polymer to swell and changing it from a glassy to rubbery state. The diffusion exponent n is the indicative of mechanism of drug release from the formulation. For a swellable drug delivery system, the n value of 0.45 is indicative of Fickian diffusion controlled drug release, n value between 0.5-0.85 signifies anomalous (non Fickian) transport, n value of 0.85 indicates case II transport, and n value greater than 0.85 indicates super case II transport. Batch F7 showed the n value 0.822 so it was signifies non Fickian transport.

**Stability Studies**

After one month of accelerated stability study (40ºC ± 2ºC and 75% RH ± 5%) of optimized batch i.e. F7, all evaluation parameters and dissolution test were performed. Results of the accelerated stability study had shown no remarkable change in the release profile of the Paroxetine HCl buccal patch after one month accelerated stability study.

**Table 18: Evaluation of optimized batch F7 (After accelerated stability study)**

| Evaluation parameters | 0 days | 30 days |
|---|---|---|
| **Tensile strength (g/mm)** | 2.0 | 1.96 |
| **Folding endurance** | >300 | >300 |
| ***Ex vivo* mucoadhesive strength (g force)** | 13.19 | 13.14 |
| **Drug content** | 100.03 | 99.97 |

**Table 19: Comparison of *in vitro* drug release study after stability study**

| Time (hr) | %CPR (initial) | %CPR (After storage at 40 ± 2 °C / 75 ± 5 %) |
|---|---|---|
| **1** | 19.18 | 18.45 |
| **2** | 27.33 | 26.47 |
| **3** | 42.47 | 43.52 |
| **4** | 57.25 | 58.41 |
| **5** | 67.29 | 68.12 |
| **6** | 78.36 | 78.61 |
| **7** | 86.71 | 84.63 |
| **8** | 99.65 | 98.57 |

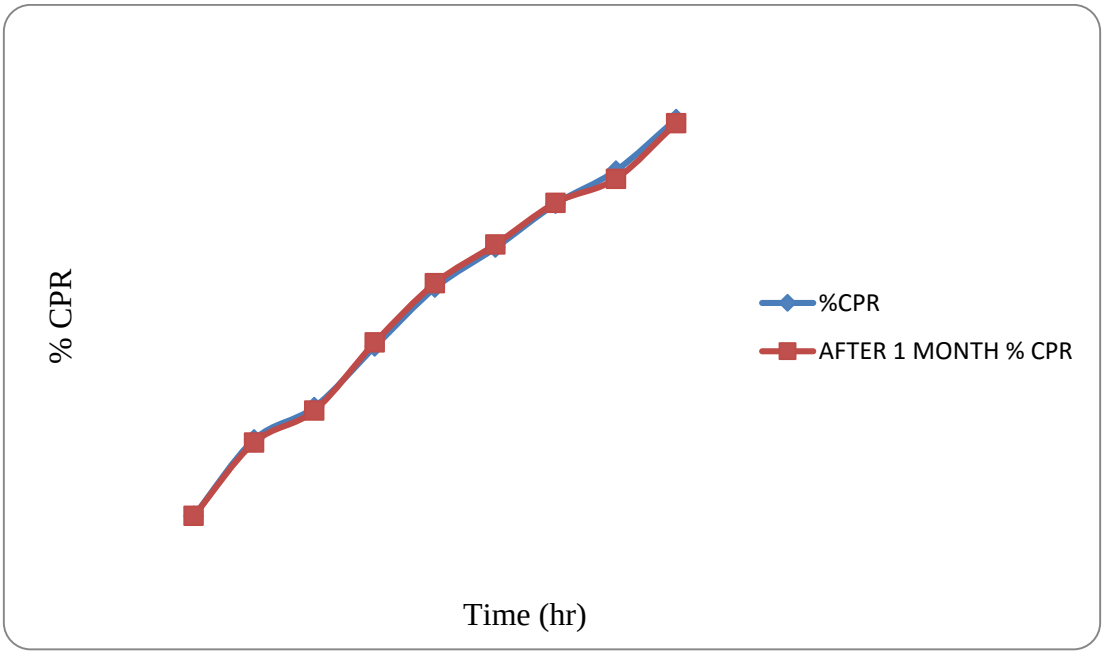


**Figure 10: Comparative dissolution profile of batch F7 initially and after one month stability**

## CONCLUSION

From this research study, it was concluded that development of bioadhesive buccal patch of Paroxetine HCl is one of the alternative drug delivery systems of administration to avoid first pass metabolism and provide prolonged release. In addition, these formulations reduce the need of frequent administration and enhance patient compliance. A combination of Xanthan gum and PVA results in controlled release buccal drug delivery. The buccal patch showed a mucoadhesion time of more than 8 h. Similarly, *ex vivo* permeation studies showed 90.45% drug permeation from the patch showing suitability of developed patch for once a day application.

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